STN Columbus

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NEWS 13  DEC 18  CA/CAplus pre-1967 chemical substance index entries enhanced
                 with preparation role
NEWS 14  DEC 18  CA/CAplus patent kind codes updated
NEWS 15  DEC 18  MARPAT to CA/CAplus accession number crossover limit increased
                 to 50,000
NEWS 16  DEC 18  MEDLINE updated in preparation for 2007 reload
NEWS 17  DEC 27  CA/CAplus enhanced with more pre-1907 records
NEWS 18  JAN 08  CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 19  JAN 16  CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 20  JAN 16  IPC version 2007.01 thesaurus available on STN
NEWS 21  JAN 16  WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS 22  JAN 22  CA/CAplus updated with revised CAS roles
NEWS 23  JAN 22  CA/CAplus enhanced with patent applications from India
NEWS 24  JAN 29  PHAR reloaded with new search and display fields
NEWS 25  JAN 29  CAS Registry Number crossover limit increased to 300,000 in
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NEWS EXPRESS  NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT
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=> s 7448-02-4
L1             1 7448-02-4
                 (7448-02-4/RN)

=> d l1 all

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   7448-02-4  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   Cholesta-8,24-dien-3-ol, 4,4-dimethyl-, (3β,5α)- (9CI)  (CA
     INDEX NAME)
OTHER CA INDEX NAMES:
CN   5α-Cholesta-8,24-dien-3β-ol, 4,4-dimethyl- (6CI, 7CI, 8CI)
OTHER NAMES:
CN   14-Norlanosterol
CN   14α-Demethyllanosterol
CN   4,4-Dimethyl-5α-cholesta-8(9),24-dien-3β-ol
CN   4,4-Dimethyl-5α-cholesta-8,24-dien-3β-ol
CN   4,4-Dimethylcholesta-8,24-dienol
CN   4,4-Dimethylzymosterol
FS   STEREOSEARCH
MF   C29 H48 O
LC   STN Files:   AGRICOLA, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS,
     CASREACT, EMBASE, MEDLINE, TOXCENTER, USPATFULL
          (*File contains numerically searchable property data)
DT.CA  CAplus document type:  Conference; Journal; Patent
RL.P   Roles from patents:  BIOL (Biological study); OCCU (Occurrence); PREP
     (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RL.NP  Roles from non-patents:  ANST (Analytical study); BIOL (Biological
     study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP
     (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
     reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents:  BIOL (Biological
     study); PREP (Preparation)

Ring System Data
```

Elemental Analysis EA	Elemental Sequence ES	Size of the Rings SZ	Ring System Formula RF	Ring Identifier RID	RID Occurrence Count
C5-C6-C6-C6	C5-C6-C6-C6	5-6-6-6	C17	4432.3.229	1

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Absolute stereochemistry.
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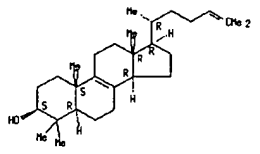

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Predicted Properties (PPROP)
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PROPERTY (CODE)	VALUE	CONDITION	NOTE
Bioconc. Factor (BCF)	1000000.0	pH 1 25 deg C	(1)
Bioconc. Factor (BCF)	1000000.0	pH 2 25 deg C	(1)
Bioconc. Factor (BCF)	1000000.0	pH 3 25 deg C	(1)
Bioconc. Factor (BCF)	1000000.0	pH 4 25 deg C	(1)
Bioconc. Factor (BCF)	1000000.0	pH 5 25 deg C	(1)
Bioconc. Factor (BCF)	1000000.0	pH 6 25 deg C	(1)
Bioconc. Factor (BCF)	1000000.0	pH 7 25 deg C	(1)
Bioconc. Factor (BCF)	1000000.0	pH 8 25 deg C	(1)
Bioconc. Factor (BCF)	1000000.0	pH 9 25 deg C	(1)
Bioconc. Factor (BCF)	1000000.0	pH 10 25 deg C	(1)
Boiling Point (BP)	495.1+/-44.0 deg C	760 Torr	(1)
Density (DEN)	0.99+/-0.1 g/cm**3	760 Torr	(1)
Enthalpy of Vap. (HVAP)	87.83+/-6.0 kJ/mol	760 Torr	(1)
Flash Point (FP)	217.7+/-20.7 deg C		(1)
Freely Rotatable Bonds (FRB)	5		(1)
H acceptors (HAC)	1		(1)
H donors (HD)	1		(1)
Hydrogen Donors/Acceptors Sum (HDAS)	2		(1)
Koc (KOC)	10000000.0	pH 1 25 deg C	(1)
Koc (KOC)	10000000.0	pH 2 25 deg C	(1)
Koc (KOC)	10000000.0	pH 3 25 deg C	(1)
Koc (KOC)	10000000.0	pH 4 25 deg C	(1)
Koc (KOC)	10000000.0	pH 5 25 deg C	(1)
Koc (KOC)	10000000.0	pH 6 25 deg C	(1)
Koc (KOC)	10000000.0	pH 7 25 deg C	(1)
Koc (KOC)	10000000.0	pH 8 25 deg C	(1)
Koc (KOC)	10000000.0	pH 9 25 deg C	(1)
Koc (KOC)	10000000.0	pH 10 25 deg C	(1)
logD (LOGD)	10.52	pH 1 25 deg C	(1)
logD (LOGD)	10.52	pH 2 25 deg C	(1)
logD (LOGD)	10.52	pH 3 25 deg C	(1)
logD (LOGD)	10.52	pH 4 25 deg C	(1)
logD (LOGD)	10.52	pH 5 25 deg C	(1)
logD (LOGD)	10.52	pH 6 25 deg C	(1)
logD (LOGD)	10.52	pH 7 25 deg C	(1)
logD (LOGD)	10.52	pH 8 25 deg C	(1)
logD (LOGD)	10.52	pH 9 25 deg C	(1)
logD (LOGD)	10.52	pH 10 25 deg C	(1)
logP (LOGP)	10.520+/-0.349	25 deg C	(1)
Mass Intrinsic Solubility (ISLB.MASS)	0.00000078 g/L	25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00000078 g/L	pH 1 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00000078 g/L	pH 2 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00000078 g/L	pH 3 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00000078 g/L	pH 4 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00000078 g/L	pH 5 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00000078 g/L	pH 6 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00000078 g/L	pH 7 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00000078 g/L	pH 8 25 deg C	(1)

Mass Solubility (SLB.MASS)	0.00000078 g/L	pH 9 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00000078 g/L	pH 10 25 deg C	(1)
Mass Solubility (SLB.MASS)	0.00000078 g/L	Unbuffered Water pH 7.00 25 deg C	(1)
Molar Intrinsic Solubility (ISLB.MOL)	0.0000000019 mol/L	25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000000019 mol/L	pH 1 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000000019 mol/L	pH 2 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000000019 mol/L	pH 3 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000000019 mol/L	pH 4 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000000019 mol/L	pH 5 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000000019 mol/L	pH 6 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000000019 mol/L	pH 7 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000000019 mol/L	pH 8 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000000019 mol/L	pH 9 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000000019 mol/L	pH 10 25 deg C	(1)
Molar Solubility (SLB.MOL)	0.0000000019 mol/L	Unbuffered Water pH 7.00 25 deg C 760 Torr	(1)
Molar Volume (MVOL)	415.9+/-5.0 cm**3/mol	20 deg C	(1)
Molecular Weight (MW)	412.69		(1)
pKa (PKA)	15.16+/-0.70	Most Acidic 25 deg C	(1)
Polar Surface Area (PSA)	20.23 A**2		(1)
Vapor Pressure (VP)	7.07E-12 Torr	25 deg C	(1)

(1) Calculated using Advanced Chemistry Development (ACD/Labs) Software V8.14 ((C) 1994-2007 ACD/Labs)

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See HELP PROPERTIES for information about property data sources in REGISTRY.
             99 REFERENCES IN FILE CA (1907 TO DATE)
              3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            100 REFERENCES IN FILE CAPLUS (1907 TO DATE)
              3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE  1
Full Text

AN   145:434527  CA
TI   Phytosterol biosynthesis pathway in Mortierella alpina
AU   Nes, W. David; Nichols, Shawn D.
CS   Department of Chemistry and Biochemistry, Texas Tech University, Lubbock,
     TX, 79409-1061, USA
SO   Phytochemistry (Elsevier) (2006), 67(16), 1716-1721
     CODEN: PYTCAS; ISSN: 0031-9422
PB   Elsevier Ltd.
DT   Journal
LA   English
CC   10-2 (Microbial, Algal, and Fungal Biochemistry)
AB   The Zygomycetes fungus Mortierella alpina was cultured to growth arrest to
     assess the phytosterol biosynthesis pathway in a less-advanced fungus.
     The mycelium was found to produce 13 sterols, but no ergosterol.  The
     sterol fractions were purified to homogeneity by HPLC and their identities
     detd. by a combination of GC-MS and 1H NMR spectroscopy.  The principal
     sterol of the mycelium was cholesta-5, 24-dienol (desmosterol) (83%), with
     lesser amts. of 24β-methyl-cholesta-5,25(27)-dienol (codisterol)
     (2%), 24-methyldesmosterol (6%), 24(28)-methylene cholesterol (3%) and
     lanosterol (3%) and several other minor compds. (3%).  The total sterol
     accounted for approx. 0.07% of the mycelial dry wt.  Mycelium fed
     methionine-methyl-2H3 for 6 days, generated 3 2H-24-methyl(ene) sterols,
     [C28-2H2]24(28)-methylenecholesterol, [C28-2H3]24-methylcholesta-5,24-
     dienol and [C28-2H3]24β-methyl-cholesta-5,25(27)-dienol.  The
     formation of the 24-Me sterols seems to be catalyzed by the direct
     methylation of a common Δ24-acceptor sterol thereby bypassing the
     intermediacy of an isomerization step for rearrangement of the
     Δ24(28)-bond to Δ25(25)-position as operates in Ascomycetes
     fungi and all plants.
ST   Mortierella phytosterol biosynthesis fungal evolution
IT   Methylation
```

(involved in phytosterol biosynthesis pathway in Mortierella alpina)
IT Mortierella alpina
(phytosterol biosynthesis pathway in Mortierella alpina)
IT Sterols
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phytosterols; phytosterol biosynthesis pathway in Mortierella alpina)
IT 57-88-5, Cholesterol, biological studies 79-62-9, 24,25-Dihydrolanosterol 79-63-0, Lanosterol 113-04-2 474-63-5 651-54-7 1715-86-2 7448-02-4 7448-03-5 20780-41-0 24778-51-6 52936-69-3, Codisterol 58801-00-6, 24-Methyl lanosterol
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(phytosterol biosynthesis pathway in Mortierella alpina)
RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD

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(27) Zhou, W; Tetrahedron Lett 1996, V37, P1339 CAPLUS

REFERENCE 2
Full Text

AN 145:99242 CA
TI Sterol uptake in Candida glabrata: Rescue of sterol auxotrophic strains

AU Bard, Martin; Sturm, Aaron M.; Pierson, Charles A.; Brown, Shaleak; Rogers, Kristina M.; Nabinger, Sarah; Eckstein, James; Barbuch, Robert; Lees, N. D.; Howell, Susan A.; Hazen, Kevin C.
CS Department of Biology, Indiana University-Purdue University Indianapolis, Indianapolis, IN, 46202, USA

SO Diagnostic Microbiology and Infectious Disease (2005), 52(4), 285-293
CODEN: DMIDDZ; ISSN: 0732-8893
PB Elsevier Inc.
DT Journal
LA English

CC 10-2 (Microbial, Algal, and Fungal Biochemistry)

AB Candida glabrata is emerging as a more common and important human pathogen. It is less susceptible to azole antifungals than Candida albicans, thus, posing some unique treatment challenges. Previously undetected C. glabrata isolates were identified from clin. specimens by adding bile to the growth medium. Cholesterol was found to be the responsible ingredient in bile. Six bile-dependent isolates were characterized and were found to exhibit wild-type equiv. growth when provided human or bovine serum or free cholesterol. Sterol profiles of the 6 isolates and a C. glabrata matching wild-type strain not requiring cholesterol indicated that 2 were defective in squalene epoxidase (encoded by the ERG1 gene) activity, 3 were defective in lanosterol synthase (encoded by the ERG7 gene) activity, and the sixth was defective in heme biosynthesis. All 7 isolates produced profiles that contained cholesterol transported from the media. Because Saccharomyces cerevisiae mutants

unable to synthesize heme will take up exogenous sterol under aerobic conditions, heme nulls of C. glabrata and C. albicans were generated and tested for growth on ergosterol media. Only the C. glabrata heme1 was able to grow indicating significant differences in exogenous sterol uptake between the 2 organisms. The ability of C. glabrata to replace ergosterol with host sterol may be responsible for its elevated azole resistance.
ST sterol; Candida heme
IT Mutation
(ERG1 mutants and ERG7 mutants of Candida glabrata clin. isolates with defective squalene epoxidase and lanosterol synthase showed exogenous cholesterol uptake ability)
IT Human
(ERG7 mutants of Candida glabrata clin. isolates with defective lanosterol synthase showed exogenous cholesterol uptake ability)
IT Microorganism
(auxotrophic; exogenous cholesterol uptake ability of ergosterol and heme auxotroph of Candida glabrata clin. isolates suggests distinct sterol uptake pathway when compared to Candida albicans)
IT Candida albicans
Candida glabrata
(exogenous cholesterol uptake ability of ergosterol and heme auxotroph of Candida glabrata clin. isolates suggests distinct sterol uptake pathway when compared to Candida albicans)
IT Gene, microbial
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(heme1; exogenous cholesterol uptake ability of ergosterol and heme auxotroph of Candida glabrata clin. isolates suggests distinct sterol uptake pathway when compared to Candida albicans)
IT Saccharomyces cerevisiae
(mutants of Saccharomyces cerevisiae with defective heme biosynthesis showed exogenous sterol uptake ability)
IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(squalene epoxidase; ERG1 mutants of Candida glabrata clin. isolates with defective squalene epoxidase showed exogenous cholesterol uptake ability)
IT 9032-71-7, Lanosterol synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ERG7 mutants of Candida glabrata clin. isolates with defective lanosterol synthase showed exogenous cholesterol uptake ability)
IT 57-87-4, Ergosterol 57-88-5, Cholesterol, biological studies 79-63-0, Lanosterol 111-02-4, Squalene 516-79-0, Ergosta-5,7-dienol 516-86-9, Fecosterol 7200-26-2, Squalene epoxide 7448-02-4, 4,4-Dimethylzymosterol 14875-96-8, Heme 16910-32-0, Obtusifoliol 31686-74-7, 14-Methyl fecosterol 131723-74-5, 4-Methyl fecosterol
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(exogenous cholesterol uptake ability of ergosterol and heme auxotroph of Candida glabrata clin. isolates suggests distinct sterol uptake pathway when compared to Candida albicans)
IT 16009-13-5, Hemin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hem1 mutants of both Candida glabrata and Candida albicans grew well with hemin and δ-ala supplementation but only C. glabrata hem1 mutant grew well with ergosterol supplementation suggesting sterol uptake of Candida glabrata)
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD

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REFERENCE 3
Full Text

AN 145:59171 CA
TI Endoplasmic reticulum-associated degradation is required for cold adaptation and regulation of sterol biosynthesis in the yeast Saccharomyces cerevisiae

AU Loertscher, Jennifer; Larson, Lynnelle L.; Matson, Clinton K.; Parrish, Mark L.; Felthauser, Alicia; Sturm, Aaron; Tachibana, Christine; Bard, Martin; Wright, Robin
CS Department of Chemistry, Seattle University, Seattle, WA, 98122, USA

SO Eukaryotic Cell (2006), 5(4), 712-722
CODEN: ECUREA2; ISSN: 1535-9778
PB American Society for Microbiology
DT Journal
LA English

CC 10-6 (Microbial, Algal, and Fungal Biochemistry)

AB Endoplasmic reticulum-assocd. degrdn. (ERAD) mediates the turnover of short-lived and misfolded proteins in the ER membrane or lumen. In spite of its important role, only subtle growth phenotypes have been assocd. with defects in ERAD. We have discovered that the ERAD proteins Ubc7 (Cpi8), Cue1, and Doa10 (Ssm4) are required for growth of yeast that express high levels of the sterol biosynthetic enzyme, 3-hydroxy-3-methylglutaryl CoA reductase (HMGR). Interestingly, the obsd. growth defect was exacerbated at low temps., producing an HMGR-dependent cold sensitivity. Yeast strains lacking UBC7, CUE1, or DOA10 also assembled aberrant karmellae (ordered arrays of membranes surrounding the nucleus that assemble when HMGR is expressed at high levels). However, rather than reflecting the accumulation of abnormal karmellae, the cold sensitivity of these ERAD mutants was due to increased HMGR catalytic activity. Mutations that compromise proteasomal function also resulted in cold-sensitive growth of yeast with elevated HMGR, suggesting that improper degrdn. of ERAD targets might be responsible for the obsd. cold-sensitive phenotype. However, the essential ERAD targets were not the yeast HMGR enzymes themselves. The sterol metabolite profile of ubc7Δ cells was altered relative to that of wild-type cells. Since sterol levels are known to regulate membrane fluidity, the viability of ERAD mutants expressing normal levels of HMGR was examd. at low temps. Cells lacking UBC7, CUE1, or DOA10 were cold sensitive, suggesting that these ERAD proteins have a role in cold adaptation, perhaps through effects on sterol biosynthesis.

ST sterol biosynthesis Ubc7 Cue1 Doa10 protein degrdn endoplasmic reticulum; ubiquitin protein proteasome ubiquitination hydroxymethylglutaryl CoA reductase Saccharomyces; cold adaptation Saccharomyces methylfecosterol dimethylzymosterol lanosterol fecosterol squalene zymosterol; episterol ergosterol Saccharomyces cold adaptation endoplasmic reticulum protein degrdn
IT Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Cue1 (Cab inderexpressed 1); endoplasmic reticulum-assocd. degrdn. is required for cold adaptation and regulation of sterol biosynthesis in yeast Saccharomyces cerevisiae)
IT Temperature effects, biological
(cold; endoplasmic reticulum-assocd. degrdn. is required for cold adaptation and regulation of sterol biosynthesis in yeast Saccharomyces cerevisiae)
IT Adaptation, microbial
Endoplasmic reticulum
Saccharomyces cerevisiae
(endoplasmic reticulum-assocd. degrdn. is required for cold adaptation and regulation of sterol biosynthesis in yeast Saccharomyces cerevisiae)
IT Sterols

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(endoplasmic reticulum-assocd. degrdn. is required for cold adaptation and regulation of sterol biosynthesis in yeast Saccharomyces cerevisiae)
IT Enzymes, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ubiquitin-conjugating, Ubc7; endoplasmic reticulum-assocd. degrdn. is required for cold adaptation and regulation of sterol biosynthesis in yeast Saccharomyces cerevisiae)
IT Protein degradation
(ubiquitination; endoplasmic reticulum-assocd. degrdn. is required for cold adaptation and regulation of sterol biosynthesis in yeast Saccharomyces cerevisiae)
IT 74812-49-0, E3 Ubiquitin ligase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Doa10/Ssm4; endoplasmic reticulum-assocd. degrdn. is required for cold adaptation and regulation of sterol biosynthesis in yeast Saccharomyces cerevisiae)
IT 57-87-4, Ergosterol 79-63-0, Lanosterol 111-02-4, Squalene 128-33-6, Zymosterol 474-68-0, Episterol 516-86-9, Fecosterol 7448-02-4, 4,4-Dimethylzymosterol 9028-35-7, 3-Hydroxy-3-methylglutaryl CoA reductase 131723-74-5, 4-Methylfecosterol 140879-24-9, Proteasome
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(endoplasmic reticulum-assocd. degrdn. is required for cold adaptation and regulation of sterol biosynthesis in yeast Saccharomyces cerevisiae)
IT 60267-61-0, Ubiquitin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ubiquitination; endoplasmic reticulum-assocd. degrdn. is required for cold adaptation and regulation of sterol biosynthesis in yeast Saccharomyces cerevisiae)
RE.CNT 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD

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REFERENCE 4
Full Text

AN 144:408262 CA
TI Lanosterol biosynthesis in plants
AU Kolesnikova, Mariya D.; Xiong, Quanbo; Lodeiro, Silvia; Hua, Ling; Matsuda, Seiichi P. T.
CS Department of Chemistry, Rice University, Houston, TX, 77005, USA
SO Archives of Biochemistry and Biophysics (2006), 447(1), 87-95
CODEN: ABBIA4; ISSN: 0003-9861
PB Elsevier
DT Journal
LA English
CC 11-2 (Plant Biochemistry)
Section cross-reference(s): 7
AB Plants biosynthesize sterols from cycloartenol using a pathway distinct from the animal and fungal route through lanosterol. Described herein are genome-mining expts. revealing that Arabidopsis encodes, in addn. to cycloartenol synthase, an accurate lanosterol synthase (LSS)-the first example of lanosterol synthases cloned from a plant. The coexistence of cycloartenol synthase and lanosterol synthase implies specific roles for both cyclopropyl and conventional sterols in plants. Phylogenetic reconstructions reveal that lanosterol synthases are broadly distributed in eudicots but evolved independently from those in animals and fungi. Novel catalytic motifs establish that plant lanosterol synthases comprise a third catalytically distinct class of lanosterol synthase.
ST lanosterol biosynthesis
IT Gene, plant
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(CAS1; lanosterol biosynthesis in plants)
IT Gene, plant
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LSS; lanosterol biosynthesis in plants)
IT Gene, plant
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(LUP1; lanosterol biosynthesis in plants)
IT Enzyme functional sites
(active; lanosterol biosynthesis in plants)
IT Protein sequences
(homol.; lanosterol biosynthesis in plants)
IT Arabidopsis thaliana
Metabolism, plant
Protein motifs
(lanosterol biosynthesis in plants)
IT Evolution
(mol., phylogeny; lanosterol biosynthesis in plants)
IT 79-63-0, Lanosterol 128-33-6, 5α-Cholesta-8,24-dien-3β-ol 474-68-0, 5α-Ergosta-7,24(28)-dien-3β-ol 516-79-0, Ergosta-5,7-dien-3β-ol 516-85-8, 22E-Ergosta-5,7,9(11),22-tetraen-3β-ol 2465-11-4, 22E-Ergosta-7,22-dien-3β-ol 5259-28-9 7448-02-4, 4,4-Dimethyl-5α-cholesta-8,24-dien-3β-ol 9032-71-7, Lanosterol synthase 9075-25-6, Cycloartenol synthase 29560-24-5 50657-31-3, 22E-Ergosta-5,8,22-trien-3β-ol
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lanosterol biosynthesis in plants)
RE.CNT 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD
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REFERENCE 5
Full Text

AN 144:370270 CA
TI Electronic and structural features of lanosterol in the 14α-demethylation
AU Cabrera-Vivas, B. M.; Pineda, Flor P.; Garcia-Hidalgo, Sandra; Melendez, P. J.; Reyes-Ortega, Y.; Ramirez, Juan Carlos
CS Facultad de Ciencias Quimicas, Centro de Quimica del Instituto de Ciencias, Benemerita Universidad Autonoma de Puebla, Puebla de Zaragoza, 72570, Mex.
SO THEOCHEM (2005), 728(1-3), 7-13
CODEN: THEODJ; ISSN: 0166-1280
PB Elsevier B.V.
DT Journal
LA English
CC 30-30 (Terpenes and Terpenoids)
Section cross-reference(s): 22
AB 14α-Demethylation is the reaction which leads directly to norlanosterol from lanosterol, and is carried out exclusively by lanosterol structure. To discover the features which make lanosterol a unique mol. able to undergo this demethylation, the electronic and energetic parameters of lanosterol and other structurally related steroids, were calcd. Local and global parameters were analyzed, in order to insight into the reactivity and selectivity of every mol. studied. Electrostatic potential maps were used to find differences of selectivity in each mol., along with total energy and hardness, discovering the differences in reactivity. Lanosterol shows specific orientation and unique shape of electrostatic potential map, which does not appear in other structures, except epilanosterol, because it differs only in the orientation of a hydroxyl group, therefore they present many similarities but many differences also. For this reason, epilanosterol has a similar shape of electrostatic potential map, but not its orientation. Aoyama et al. have found, three essential structural features in lanosterol to be demethylated, which generate a specific electrostatic potential map, the hydroxyl group on C-3, the position of the double bound between C8 and C9 on cycle B, and the side chain double bond. Our study agrees with some biochem. studies, which reveal that there are three key features essential for substrate recognition by the enzyme P 45014DM. We think the present study is an alternative methodol. to find features which are related with some parameters obtained via theor. calcns.
ST lanosterol demethylation electrostatic potential energy hardness calcn
IT Demethylation
Electrostatic potential energy surface
Hardness (electronic structure)
Total energy
(electronic and structural calcns. of lanosterol in 14α-demethylation)
IT 79-63-0, Lanosterol 2671-68-3 5539-04-8, Lanosta-8,24-dien-3-one 7408-46-0 7427-64-7 7448-02-4, 14α-Demethyllanosterol 76582-59-7, 3-Epilanosterol 882493-98-3 882493-99-4 882494-00-0
RL: PRP (Properties)
(electronic and structural calcns. of lanosterol in 14α-demethylation)
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
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REFERENCE 6
Full Text

AN 144:366161 CA
TI Aspergillus fumigatus C-5 sterol desaturases Erg3A and Erg3B: role in sterol biosynthesis and antifungal drug susceptibility
AU Alcazar-Fuoli, Laura; Mellado, Emilia; Garcia-Effron, Guillermo; Buitrago, Maria J.; Lopez, Jordi F.; Grimalt, Joan O.; Cuenca-Estrella, J. Manuel; Rodriguez-Tudela, Juan L.
CS Servicio de Micologia, Centro Nacional de Microbiologia, Instituto de Salud Carlos III, Madrid, Spain
SO Antimicrobial Agents and Chemotherapy (2006), 50(2), 453-460
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
CC 10-2 (Microbial, Algal, and Fungal Biochemistry)
AB Two erg1 genes encoding C-5 sterol desaturase enzymes (Erg3A and Erg3B) in Aspergillus fumigatus were characterized with respect to their nucleotide sequences, null mutant phenotypes. Targeted disruption of the erg3A and erg3B genes and a double gene knockout, erg3A- erg3B-, showed that they are not essential for A. fumigatus viability. Mutant phenotypes clearly showed that Erg3B is a C-5 sterol desaturase, but no apparent role for Erg3A in A. fumigatus ergosterol biosynthesis was found. Susceptibility to amphotericin B, itraconazole, fluconazole, voriconazole, and ketoconazole was not altered in isolates in which erg3A and erg3B were knocked out alone and in combination.
ST Aspergillus sterol desaturase sequence sterol biosynthesis antifungal susceptibility
IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(erg3A; role of Aspergillus fumigatus C-5 sterol desaturases Erg3A and Erg3B in sterol biosynthesis and antifungal drug susceptibility)
IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(erg3B; role of Aspergillus fumigatus C-5 sterol desaturases Erg3A and Erg3B in sterol biosynthesis and antifungal drug susceptibility)
IT Gene, microbial
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(erg3C; role of Aspergillus fumigatus C-5 sterol desaturases Erg3A and Erg3B in sterol biosynthesis and antifungal drug susceptibility)
IT Protein sequences

(homol.; role of Aspergillus fumigatus C-5 sterol desaturases Erg3A and Erg3B in sterol biosynthesis and antifungal drug susceptibility)
IT Aspergillus fumigatus
DNA sequences
Fungicide resistance
Protein sequences
(role of Aspergillus fumigatus C-5 sterol desaturases Erg3A and Erg3B in sterol biosynthesis and antifungal drug susceptibility)
IT Sterols
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(role of Aspergillus fumigatus C-5 sterol desaturases Erg3A and Erg3B in sterol biosynthesis and antifungal drug susceptibility)
IT 881728-58-1 881728-60-5 881728-62-7
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; role of Aspergillus fumigatus C-5 sterol desaturases Erg3A and Erg3B in sterol biosynthesis and antifungal drug susceptibility)
IT 881728-57-0 881728-59-2 881728-61-6
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; role of Aspergillus fumigatus C-5 sterol desaturases Erg3A and Erg3B in sterol biosynthesis and antifungal drug susceptibility)
IT 57-87-4, Ergosterol 79-63-0, Lanosterol 474-68-0, Episterol 516-85-8 1397-89-3, Amphotericin B 6890-88-6, Eburicol 7448-02-4 14250-23-8 21674-20-4, 24-Ethylcholesta-5,7,22-trien-3β-ol 23582-83-4 29560-24-5 36680-39-4 41388-21-0, 24-Methylcholesta-7,22-dien-3β-ol 50657-31-3, Lichesterol 65277-42-1, Ketoconazole 84625-61-6, Itraconazole 86386-73-4, Fluconazole 137234-62-9, Voriconazole
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(role of Aspergillus fumigatus C-5 sterol desaturases Erg3A and Erg3B in sterol biosynthesis and antifungal drug susceptibility)
IT 162874-99-9
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(role of Aspergillus fumigatus C-5 sterol desaturases Erg3A and Erg3B in sterol biosynthesis and antifungal drug susceptibility)
RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD

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REFERENCE 7
Full Text

AN 144:167035 CA
TI A systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system
AU Mo, Caiqing; Bard, Martin
CS Department of Biology, Indiana University-Purdue University Indianapolis, Indianapolis, IN, 46202, USA
SO Biochimica et Biophysica Acta, Molecular and Cell Biology of Lipids (2005), 1737(2-3), 152-160
CODEN: BBMLFG; ISSN: 1388-1981
PB Elsevier B.V.
DT Journal
LA English
CC 10-2 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 7
AB Sterol biosynthesis occurs in the ER and most sterol biosynthetic enzymes have transmembrane domains. However, due to difficulties in characterizing membrane protein-protein interactions, the nature of the sterol biosynthetic complex as well as in vivo interactions between various enzymes have not been described. We employed a split-ubiquitin membrane protein yeast two-hybrid system to characterize interactions between sterol biosynthetic proteins. Fourteen bait constructs were co-transformed into a reporter yeast strain with 14 prey constructs representing all sterol enzymic reactions beginning with the synthesis of squalene. Our results not only confirmed several previous interactions, but also allowed us to identify novel interactions. Based on these results, ergosterol biosynthetic enzymes display specific protein-protein interactions forming a functional complex we designate, the ergosome. In this complex, Erg11p, Erg25p, Erg27p, and Erg28p appear to form a core center that can interact with other enzymes in the pathway. Also Erg24p and Erg2p, two enzymes that are sensitive to morpholine antifungals, appear to interact with one another; however, the profile of protein interaction partners appears to be unique. Erg2p and Erg3p, two enzymes catalyzing sequential reactions also appear to have different interaction partners. Our results provide a working model as to how sterol biosynthetic enzymes are topol. organized not only in yeast but in plant and animal systems that share many of these biosynthetic reactions.
ST sterol biosynthesis enzyme assocn yeast
IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(complexes; systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system)
IT Protein-protein interaction
Ribosome
Yeast
(systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system)
IT 60063-87-8, Lanosterol C-14 demethylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ERG11; systematic study of yeast sterol biosynthetic protein-protein

interactions using the split-ubiquitin system)
IT 9029-62-3, Squalene epoxidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ERG1; systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system)
IT 69403-07-2, Sterol C-14 reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ERG24; systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system)
IT 42616-26-2, 4-Methyl Sterol oxidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ERG25; systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system)
IT 130590-42-0, 4α-Carboxysterol-C3 dehydrogenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ERG26; systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system)
IT 9028-40-4, 3-Keto reductase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ERG27; systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system)
IT 52410-46-5, C-8 Sterol isomerase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ERG2; systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system)
IT 162874-99-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ERG3; systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system)
IT 110183-45-4
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ERG5; systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system)
IT 37257-07-1, Sterol C-24 methyltransferase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ERG6; systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system)
IT 9032-71-7, Lanosterol synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ERG7; systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system)
IT 9077-14-9, Squalene synthase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(ERG9; systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system)
IT 9033-57-2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Sterol C-24 reductase, ERG4; systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system)
IT 57-87-4, Ergosterol 79-63-0, Lanosterol 111-02-4, Squalene 128-33-6, Zymosterol 474-68-0, Episterol 516-86-9, Fecosterol 7200-26-2, Squalene epoxide 7448-02-4, 4,4-Dimethylzymosterol 29560-24-5 64284-64-6, 4,4-Dimethyl-5α-cholesta-8,14,24-trien-3β-ol
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system)
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD

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REFERENCE 8
Full Text

AN 142:351946 CA
TI Disruption of ergosterol biosynthesis, growth, and the morphological transition in Candida albicans by sterol methyltransferase inhibitors containing sulfur at C-25 in the sterol side chain
AU Kanagasabai, Ragu; Zhou, Wenxu; Liu, Jialin; Nguyen, Thi Thuy Minh; Veeramachaneni, Phani; Nes, W. David
CS Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, TX, 79409, USA
SO Lipids (2004), 39(8), 737-746
CODEN: LPDSAP; ISSN: 0024-4201
PB AOCS Press
DT Journal
LA English
CC 10-5 (Microbial, Algal, and Fungal Biochemistry)
Section cross-reference(s): 1, 32
AB The sterol substrate analog 25-thialanosterol and its corresponding sulfonium salt were evaluated for their ability to serve as antifungal agents and to inhibit sterol methyltransferase (SMT) activity in Candida albicans. Both compds. inhibited cell proliferation, were fungistatic, interrupted the yeast-like-form to germ-tube-form transition, and resulted in the accumulation of zymosterol and related Δ24-sterols concurrent with a decrease in ergosterol, as was expected for the specific inhibition of SMT activity. Feedback control on sterol synthesis was evidenced by elevated levels of cellular sterols in treated vs. control cultures. However, neither farnesol nor squalene accumulated in significant amts. in treated cultures, suggesting that carbon flux is channeled from the isoprenoid pathway to the sterol pathway with minor interruption or redirection until blockage at the C-methylation step. Activity assays using solubilized C. albicans SMT confirmed the inhibitors impair SMT action. Kinetic anal. indicated that 25-thialanosterol inhibited SMT with the properties of a time-dependent mechanism-based inactivator Ki of 5 μM and apparent kinact of 0.013 min-1, whereas the corresponding sulfonium salt was a reversible-type transition state analog exhibiting a Ki of 20 nM. The results are interpreted to imply changes in ergosterol homeostasis as influenced by SMT activity can control growth and the morphol. transition in C. albicans, possibly affecting disease development.
ST Candida sterol methyltransferase inhibitor thialanosterol
IT Candida albicans
Fungicides
(disruption of ergosterol biosynthesis, growth, and morphol. transition in Candida albicans by sterol methyltransferase inhibitors contg. sulfur at C-25 in sterol side chain)
IT Sterols
RL: BSU (Biological study, unclassified); CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(disruption of ergosterol biosynthesis, growth, and morphol. transition

in Candida albicans by sterol methyltransferase inhibitors contg. sulfur at C-25 in sterol side chain)

IT Enzyme kinetics
(of inhibition; disruption of ergosterol biosynthesis, growth, and morphol. transition in Candida albicans by sterol methyltransferase inhibitors contg. sulfur at C-25 in sterol side chain)

IT 57-87-4, Ergosterol 128-33-6, Zymosterol 516-79-0, Ergosta-5,7-dienol 516-86-9, Fecosterol 651-54-7 1715-86-2 5259-28-9, Ergosta-8-enol 6890-88-6, Episterol 7448-02-4, 4,4-Dimethylcholesta-8,24-dienol 17105-77-0 26047-31-4 34298-92-5 37257-07-1 56297-93-9 65982-33-4 224566-30-7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(disruption of ergosterol biosynthesis, growth, and morphol, transition in Candida albicans by sterol methyltransferase inhibitors contg. sulfur at C-25 in sterol side chain)

IT 848945-64-2P
RL: BSU (Biological study, unclassified); CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(disruption of ergosterol biosynthesis, growth, and morphol. transition in Candida albicans by sterol methyltransferase inhibitors contg. sulfur at C-25 in sterol side chain)

IT 79-63-0, Lanosterol
RL: BSU (Biological study, unclassified); CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
(disruption of ergosterol biosynthesis, growth, and morphol. transition in Candida albicans by sterol methyltransferase inhibitors contg. sulfur at C-25 in sterol side chain)

IT 848945-66-4P
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(disruption of ergosterol biosynthesis, growth, and morphol. transition in Candida albicans by sterol methyltransferase inhibitors contg. sulfur at C-25 in sterol side chain)

IT 5672-71-9P 27863-27-0P 848945-62-0P
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(disruption of ergosterol biosynthesis, growth, and morphol. transition in Candida albicans by sterol methyltransferase inhibitors contg. sulfur at C-25 in sterol side chain)

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REFERENCE 9
Full Text

AN 141:243721 CA
TI Efficient routes to epimerically-pure side-chain derivatives of lanosterol
AU Kavtaradze, Levan K.; Manley-Harris, Merilyn; Nicholson, Brian K.
CS Department of Chemistry, University of Waikato, Hamilton, 3105, N. Z.
SO Steroids (2004), 69(4), 227-233
CODEN: STEDAM; ISSN: 0039-128X
PB Elsevier Science B.V.
DT Journal
LA English
CC 32-7 (Steroids)
AB A tech. simple route is described to individual epimers of side-chain derivs. of lanosterol (3β-hydroxy-5α-lanosta-8,24-diene). Epimerically pure 24,25-epoxy- 24,25-dihydroxy- and 24-bromo-25-hydroxy-lanosterol have been prepd. in good yield from com. (50-60%) lanosterol. Hypophosphorous acid was used as a catalyst for the cohalogenation of the Δ24(25) bond and also for the efficient conversion of 24,25-epoxy- and 24-bromo-25-hydroxylanosterol to epimerically pure 24(R) or 24(S)-24,25-dihydroxylanosterols.
ST lanosterol deriv prepn
IT 5241-24-7 7448-02-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of lanosterol derivs.)
IT 7408-46-0P 752998-39-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of lanosterol derivs.)
IT 5241-26-9P 752998-37-1P 752998-40-6P 752998-41-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of lanosterol derivs.)
IT 752998-36-0P 752998-38-2P 752998-43-9P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of lanosterol derivs. and crystal structure)
IT 752998-42-8P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of lanosterol derivs. and crystal structure)
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD

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REFERENCE 10
Full Text

AN 140:300853 CA
TI A functional cytochrome P450 lanosterol 14α-demethylase CYP51 enzyme in the acrosome: Transport through the golgi and synthesis of meiosis-activating sterols
AU Cotman, M.; Jezek, D.; Tacer, K. Fon; Frangez, R.; Rozman, D.
CS Laboratory for Genetics, Veterinary Faculty, University of Ljubljana, Ljubljana, SI-1000, Slovenia
SO Endocrinology (2004), 145(3), 1419-1426
CODEN: ENDOAO; ISSN: 0013-7227
PB Endocrine Society
DT Journal
LA English
CC 13-1 (Mammalian Biochemistry)
AB Mammalian lanosterol 14α-demethylase (CYP51) is a microsomal cytochrome P 450 that demethylates lanosterol to FF-MAS, an oocyte meiosis-activating sterol and late intermediate of cholesterol biosynthesis. Herein the authors report CYP51 unequivocally localized to acrosomal membranes of male germ cells in mouse, bull, and ram, in which it synthesizes FF-MAS in the presence of the acrosomal form of NADP reduced-P 450 reductase. In the mouse, CYP51 (53 kDa) resides in endoplasmic reticulum (ER) and Golgi during all phases of acrosome development, indicating an intracellular transport from ERs through the Golgi to the acrosome. CYP51 (50 kDa) also resides on acrosomal membranes of bull- and ram-ejaculated sperm. In mouse liver, a 53-kDa CYP51 is no longer detected in trans Golgi, suggesting retrieval back to the ER and no further transport to other organelles. Glycosylated high-mol.-mass CYP51-immunoreactive proteins in acrosomal membranes of bull and ram and Golgi-enriched fractions of mouse liver indicate that mammalian CYP51s are subjected to post-translational modifications in the Golgi. In conclusion, CYP51 is the first cytochrome P 450 enzyme to be detected on acrosomal membranes. It exhibits a unique, cell-type-specific intracellular transport that is in agreement with its cell-type-specific physiol. role: prodn. of cholesterol in the liver and sterols with signaling properties in sperm. Demethylation of lanosterol to FF-MAS by the acrosomal lanosterol 14α-demethylase enzyme complex demonstrates for the first time the ability of ejaculate sperm to synthesize meiosis-activating sterols.
ST CYP51 lanosterol demethylase acrosome transport golgi meiosis activating sterol; NADPH cytochrome P450 reductase lanosterol demethylase CYP51 acrosome sperm
IT Sperm
(acrosome; functional cytochrome P 450 lanosterol 14α-demethylase CYP51 enzyme in acrosome in relation to transport through golgi and synthesis of meiosis-activating sterols as evaluated in mouse liver and testis)
IT Meiosis
(activating sterols; functional cytochrome P 450 lanosterol 14α-demethylase CYP51 enzyme in acrosome in relation to transport through golgi and synthesis of meiosis-activating sterols as evaluated in mouse liver and testis)
IT Demethylation
Endoplasmic reticulum
Golgi apparatus
Post-translational processing
Reproduction, animal
Testis
(functional cytochrome P 450 lanosterol 14α-demethylase CYP51 enzyme in acrosome in relation to transport through golgi and synthesis of meiosis-activating sterols as evaluated in mouse liver and testis)
IT Liver
(hepatocyte; functional cytochrome P 450 lanosterol 14α-demethylase CYP51 enzyme in acrosome in relation to transport through golgi and synthesis of meiosis-activating sterols as evaluated in mouse liver and testis)
IT Biological transport
(intracellular; functional cytochrome P 450 lanosterol 14α-demethylase CYP51 enzyme in acrosome in relation to transport through golgi and synthesis of meiosis-activating sterols as evaluated in mouse liver and testis)
IT Sterols
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(meiosis-activating; functional cytochrome P 450 lanosterol 14α-demethylase CYP51 enzyme in acrosome in relation to transport through golgi and synthesis of meiosis-activating sterols as evaluated in mouse liver and testis)
IT Sperm
(spermatid; functional cytochrome P 450 lanosterol 14α-demethylase CYP51 enzyme in acrosome in relation to transport through golgi and synthesis of meiosis-activating sterols as evaluated in mouse liver and testis)
IT 57-88-5, Cholesterol, biological studies 79-62-9, 24,25-Dihydrolanosterol 79-63-0, Lanosterol 7448-02-4 9039-06-9, NADPH cytochrome P450 reductase 60063-87-8, Lanosterol 14α-demethylase 64284-64-6, FF-MAS 440356-80-9, Cytochrome P 450 51
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(functional cytochrome P 450 lanosterol 14α-demethylase CYP51 enzyme in acrosome in relation to transport through golgi and synthesis of meiosis-activating sterols as evaluated in mouse liver and testis)
RE.CNT 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD

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=> d 12

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ED Entered STN: 16 Nov 1984
CN Cholesta-8,24-dien-3-ol, (3β,5α)- (9CI) (CA INDEX NAME)
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CN 5α-Cholesta-8,24-dien-3β-ol (8CI)
OTHER NAMES:
CN Cholest-8,24-dien-3β-ol
CN Zymosterol
FS STEREOSEARCH
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LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CHEMLIST, CSCHEM, EMBASE, MEDLINE, NAPRALERT, SPECINFO, TOXCENTER, USPATFULL
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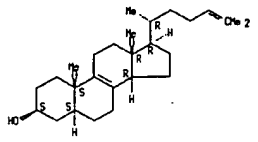

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L4 ANSWER 1 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2006:406923 CAPLUS
DOCUMENT NUMBER: 145:59171
TITLE: Endoplasmic reticulum-associated degradation is required for cold adaptation and regulation of sterol biosynthesis in the yeast Saccharomyces cerevisiae
AUTHOR(S): Loertscher, Jennifer; Larson, Lynnelle L.; Matson, Clinton K.; Parrish, Mark L.; Felthauser, Alicia; Sturm, Aaron; Tachibana, Christine; Bard, Martin; Wright, Robin
CORPORATE SOURCE: Department of Chemistry, Seattle University, Seattle, WA, 98122, USA
SOURCE: Eukaryotic Cell (2006), 5(4), 712-722
CODEN: ECUEA2; ISSN: 1535-9778
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Endoplasmic reticulum-assocd. degrdn. (ERAD) mediates the turnover of short-lived and misfolded proteins in the ER membrane or lumen. In spite of its important role, only subtle growth phenotypes have been assocd. with defects in ERAD. We have discovered that the ERAD proteins Ubc7 (Qri8), Cue1, and Doa10 (Ssm4) are required for growth of yeast that express high levels of the sterol biosynthetic enzyme, 3-hydroxy-3-methylglutaryl CoA reductase (HMGR). Interestingly, the obsd. growth defect was exacerbated at low temps., producing an HMGR-dependent cold sensitivity. Yeast strains lacking UBC7, CUE1, or DOA10 also assembled aberrant karmellae (ordered arrays of membranes surrounding the nucleus that assemble when HMGR is expressed at high levels). However, rather than reflecting the accumulation of abnormal karmellae, the cold sensitivity of these ERAD mutants was due to increased HMGR catalytic activity. Mutations that compromise proteasomal function also resulted in cold-sensitive growth of yeast with elevated HMGR, suggesting that improper degrdn. of ERAD targets might be responsible for the obsd. cold-sensitive phenotype. However, the essential ERAD targets were not the yeast HMGR enzymes themselves. The sterol metabolite profile of ubc7Δ cells was altered relative to that of wild-type cells. Since sterol levels are known to regulate membrane fluidity, the viability of ERAD mutants expressing normal levels of HMGR was exam. at low temps. Cells lacking UBC7, CUE1, or DOA10 were cold sensitive, suggesting that these ERAD proteins have a role in cold adaptation, perhaps through effects on sterol biosynthesis.
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2006:951546 CAPLUS
TITLE: Metabolic flux analysis of the sterol pathway in the yeast Saccharomyces cerevisiae
AUTHOR(S): Maczek, Judith; Junne, Stefan; Nowak, Peter; Goetz, Peter
CORPORATE SOURCE: Department of Bioprocess Engineering, Institute of Biotechnology, Technical University of Berlin, Berlin, 13355, Germany
SOURCE: Bioprocess and Biosystems Engineering (2006), 29(4), 241-252
CODEN: BBEIBV; ISSN: 1615-7591
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal

LANGUAGE: English
AB The yeast Saccharomyces cerevisiae is a useful model system for examg. the biosynthesis of sterols in eukaryotic cells. To investigate underlying regulation mechanisms, a flux anal. of the ergosterol pathway was performed. A stoichiometric model was derived based on well known biochem. of the pathway. The model was integrated in the Software COMPFlux which uses a global optimization algorithm for the estn. of intracellular fluxes. Sterol concn. patterns were detd. by gas chromatog. in aerobic and anaerobic batch cultivations, when the sterol metab. was suppressed due to the absence of oxygen. In addn., the sterol concns. were obsd. in a cultivation which was shifted from anaerobic to aerobic growth conditions causing the sterol pools in the cell to be filled. From time-dependent flux patterns, possible limitations in the pathway could be localized and the esterification of sterols was identified as an integral part of regulation in ergosterol biosynthesis.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2006:206219 CAPLUS
DOCUMENT NUMBER: 144:408262
TITLE: Lanosterol biosynthesis in plants
AUTHOR(S): Kolesnikova, Mariya D.; Xiong, Quanbo; Lodeiro, Silvia; Hua, Ling; Matsuda, Seiichi P. T.
CORPORATE SOURCE: Department of Chemistry, Rice University, Houston, TX, 77005, USA
SOURCE: Archives of Biochemistry and Biophysics (2006), 447(1), 87-95
CODEN: ABBIA4; ISSN: 0003-9861
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Plants biosynthesize sterols from cycloartenol using a pathway distinct from the animal and fungal route through lanosterol. Described herein are genome-mining expts. revealing that Arabidopsis encodes, in addn. to cycloartenol synthase, an accurate lanosterol synthase (LSS)-the first example of lanosterol synthases cloned from a plant. The coexistence of cycloartenol synthase and lanosterol synthase implies specific roles for both cyclopropyl and conventional sterols in plants. Phylogenetic reconstructions reveal that lanosterol synthases are broadly distributed in eudicots but evolved independently from those in animals and fungi. Novel catalytic motifs establish that plant lanosterol synthases comprise a third catalytically distinct class of lanosterol synthase.
REFERENCE COUNT: 86 THERE ARE 86 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 40 AGRICOLA Compiled and distributed by the National
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ACCESSION NUMBER: 2005:84571 AGRICOLA
DOCUMENT NUMBER: IND43754262
TITLE: Characterizing Sterol Defect Suppressors Uncovers a Novel Transcriptional Signaling Pathway Regulating Zymosterol Biosynthesis.
AUTHOR(S): Germann, Melody; Gallo, Christina; Donahue, Timothy; Shirzadi, Reza; Stukey, Joseph; Lang, Silvia; Ruckenstuhl, Christoph; Oliaro-Bosso, Simonetta; McDonough, Virginia; Turnowsky, Friederike; Balliano, Gianni; Nickels, Joseph T.
SOURCE: Journal of biological chemistry, 2005 Oct. 28 Vol. 280, no. 43 p. 35904-35913
ISSN: 0021-9258
NOTE: Includes references
DOCUMENT TYPE: Article
FILE SEGMENT: Other US
LANGUAGE: English
AB erg26-1[superscript ts] cells harbor defects in the 4[alpha]-carboxysterol-C3 dehydrogenase activity necessary for conversion of 4,4-dimethylzymosterol to zymosterol. Mutant cells accumulate toxic

4-carboxysterols and are inviable at high temperature. A genetic screen aimed at cloning recessive mutations remediating the temperature sensitive growth defect has resulted in the isolation of four complementation groups, ets1-4 (erg26-1[superscript ts]) temperature sensitive suppressor). We describe the characterization of ets1-1 and ets2-1. Gas chromatography/mass spectrometry analyses demonstrate that erg26-1[superscript ts] ets1-1 and erg26-1[superscript ts] ets2-1 cells do not accumulate 4-carboxysterols, rather these cells have increased levels of squalene and squalene epoxide, respectively. ets1-1 and ets2-1 cells accumulate these same sterol intermediates. Chromosomal integration of ERG1 ERG7 at their loci in erg26-1[superscript ts] ets1-1 and erg26-1[superscript ts] and ets2-1 mutants, respectively, results in the loss of accumulation of squalene and squalene epoxide, re-accumulation of 4-carboxysterols and cell inviability at high temperature. Enzymatic assays demonstrate that mutants harboring the ets1-1 allele have decreased squalene epoxidase activity, while those containing the ets2-1 allele show weakened oxidosqualene cyclase activity. Thus, ETS1 and ETS2 are allelic to ERG1 and ERG7, respectively. We have mapped mutations within the erg1-1/ets1-1 (G247D) and erg7-1/ets2-1 (D530N, V615E) alleles that suppress the inviability of erg26-1[superscript ts] at high temperature, and cause accumulation of sterol intermediates and decreased enzymatic activities. Finally using erg1-1 and erg7-1 mutant strains, we demonstrate that the expression of the ERG25/26/27 genes required for zymosterol biosynthesis are coordinately transcriptionally regulated, along with ERG1 and ERG7, in response to blocks in sterol biosynthesis. Transcriptional regulation requires the transcription factors, Upc2p and Ecm22p.

L4 ANSWER 5 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2005:1300505 CAPLUS
DOCUMENT NUMBER: 144:167035
TITLE: A systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system
AUTHOR(S): Mo, Caiqing; Bard, Martin
CORPORATE SOURCE: Department of Biology, Indiana University-Purdue University Indianapolis, Indianapolis, IN, 46202, USA
SOURCE: Biochimica et Biophysica Acta, Molecular and Cell Biology of Lipids (2005), 1737(2-3), 152-160
CODEN: BBMLFQ; ISSN: 1388-1981
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sterol biosynthesis occurs in the ER and most sterol biosynthetic enzymes have transmembrane domains. However, due to difficulties in characterizing membrane protein-protein interactions, the nature of the sterol biosynthetic complex as well as in vivo interactions between various enzymes have not been described. We employed a split-ubiquitin membrane protein yeast two-hybrid system to characterize interactions between sterol biosynthetic proteins. Fourteen bait constructs were co-transformed into a reporter yeast strain with 14 prey constructs representing all sterol enzymic reactions beginning with the synthesis of squalene. Our results not only confirmed several previous interactions, but also allowed us to identify novel interactions. Based on these results, ergosterol biosynthetic enzymes display specific protein-protein interactions forming a functional complex we designate, the ergosome. In this complex, Erg11p, Erg25p, Erg27p, and Erg28p appear to form a core center that can interact with other enzymes in the pathway. Also Erg24p and Erg2p, two enzymes that are sensitive to morpholine antifungals, appear to interact with one another; however, the profile of protein interaction partners appears to be unique. Erg2p and Erg3p, two enzymes catalyzing sequential reactions also appear to have different interaction partners. Our results provide a working model as to how sterol biosynthetic enzymes are topol. organized not only in yeast but in plant and animal systems that share many of these biosynthetic reactions.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2004:1102525 CAPLUS
DOCUMENT NUMBER: 142:351946

TITLE: Disruption of ergosterol biosynthesis, growth, and the morphological transition in Candida albicans by sterol methyltransferase inhibitors containing sulfur at C-25 in the sterol side chain
AUTHOR(S): Kanagasabai, Ragu; Zhou, Wenxu; Liu, Jialin; Nguyen, Thi Thuy Minh; Veeramachaneni, Phani; Nes, W. David
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, TX, 79409, USA
SOURCE: Lipids (2004), 39(8), 737-746
CODEN: LPDSAP; ISSN: 0024-4201
PUBLISHER: AOCS Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The sterol substrate analog 25-thialanosterol and its corresponding sulfonium salt were evaluated for their ability to serve as antifungal agents and to inhibit sterol methyltransferase (SMT) activity in Candida albicans. Both compds. inhibited cell proliferation, were fungistatic, interrupted the yeast-like-form to germ-tube-form transition, and resulted in the accumulation of zymosterol and related Δ24-sterols concurrent with a decrease in ergosterol, as was expected for the specific inhibition of SMT activity. Feedback on sterol synthesis was evidenced by elevated levels of cellular sterols in treated vs. control cultures. However, neither farnesol nor squalene accumulated in significant amts. in treated cultures, suggesting that carbon flux is channeled from the isoprenoid pathway to the sterol pathway with minor interruption or redirection until blockage at the C-methylation step. Activity assays using solubilized C. albicans SMT confirmed the inhibitors impair SMT action. Kinetic anal. indicated that 25-thialanosterol inhibited SMT with the properties of a time-dependent mechanism-based inactivator Ki of 5 μM and apparent kinact of 0.013 min-1, whereas the corresponding sulfonium salt was a reversible-type transition state analog exhibiting a Ki of 20 nM. The results are interpreted to imply changes in ergosterol homeostasis as influenced by SMT activity can control growth and the morphol. transition in C. albicans, possibly affecting disease development.
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ACCESSION NUMBER: 2003:5486 CAPLUS
DOCUMENT NUMBER: 138:56133
TITLE: Preparation of steroid imidazo heterobicycle derivatives as factor Xa inhibitors
INVENTOR(S): Byskov, Anne G.; Andersen, Claus Y.; Nordholm, Lars; Thogersen, Henning; Wasaman, Ole; Diers, Ivan Verner; Ouddahl, Erling
PATENT ASSIGNEE(S): Den.
SOURCE: U.S. Pat. Appl. Publ., 13 pp., Cont.-in-part of U.S. Ser. No. 440,590, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003004148	A1	20030102	US 2002-58436	20020123
US 5716777	A	19980210	US 1995-448217	19950523
ZA 9505213	A	19960315	ZA 1995-5213	19950623
US 2005222098	A1	20051006	US 2005-131483	20050518
PRIORITY APPLN. INFO.:			DK 1994-753 A	19940623
			DK 1995-241 A	19950309
			US 1995-448217 A1	19950523
			US 1998-17087 B2	19980202
			US 1999-440590 B2	19991115
			US 2002-58436 B1	20020123

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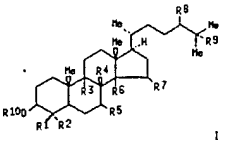

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AB Compds. I [R1, R2 = H, (un)branched C1-6-alkyl, C1-6-haloalkyl, C1-6-hydroxyalkyl; R1R2 = cyclopentane, cyclohexane ring; R3R4 = bond, where R5 = H, R6R7 = bond or R6 = R7 = H; R4R5 = bond, where R3 = H, R6R7 = bond or R6 = R7 = H; R4R6 = bond, R3 = R5 = R7 = H; R8 = R9 = H; R8R9 = bond; R10 = H, acyl, sulfo, phosphono] and methods of regulating the meiosis in a mammalian germ cell which method comprises administering an effective amt. of the compd. I to a germ cell in need of such a treatment. Thus, 4β-methylzymosterol (I; R1 = Me, R2 = R5 - R7 = R10 = H, R3R4 = R8R9 = bond) was prepd. from sodium deoxycholate via biotransformation with Kluyveromyces bulgaricus. I were tested for their MIS activity [2.7 MIS units vs. denuded oocytes and 2.9 MIS units vs. cumulus enclosed oocytes at 1.2μg/mL; and pos. activity at 10μg/mL vs. gonads for 4,4-dimethylzymosterol I (R1 = R2 = Me, R3R4 = R8R9 = bond, R5 - R7 = R10 = H)].

L4 ANSWER 8 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2003:589448 CAPLUS
DOCUMENT NUMBER: 139:148556
TITLE: Manufacture of 7-Dehydrocholesterol and its metabolites in transgenic microorganisms expressing genes for enzymes of steroid metabolism
INVENTOR(S): Lang, Christine; Veen, Markus
PATENT ASSIGNEE(S): BASF AG, Germany
SOURCE: Ger. Offen., 120 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10203352	A1	20030731	DE 2002-10203352	20020129
WO 2003064650	A1	20030807	WO 2003-EP592	20030122
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1472354	A1	20041103	EP 2003-701537	20030122
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
US 2006240508	A1	20061026	US 2004-503044	20040729
PRIORITY APPLN. INFO.:			DE 2002-10203352 A	20020129
			WO 2003-EP592 W	20030122

AB 7-Dehydrocholesterol or its metabolites are manufd. in transgenic microorganisms expressing foreign genes for enzymes of steroid metab. Furthermore, the invention concerns nucleic acid constructs, as well as genetically changed organisms needed for prodn. of genetically changed organisms, in particular yeasts. A series of integrating expression constructs carrying Saccharomyces cerevisiae or mouse genes for enzymes of steroid metab., including Δ8,7 isomerase, Δ5 desaturase and

Δ24 reductases were constructed and introduced into a yeast host. Several different combinations of these genes were expressed in a Saccharomyces cerevisiae. Qual. changes in patterns of steroid biosynthesis were obsd. with different combination of genes with novel steroids appearing in the hosts.

L4 ANSWER 9 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2003:589447 CAPLUS
DOCUMENT NUMBER: 139:148555
TITLE: Manufacture of zymosterol and its metabolites using microorganisms with increased lanosterol demethylase and HMG CoA reductase activity
PATENT ASSIGNEE(S): BASF AG, Germany
SOURCE: Ger. Offen., 44 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10203346	A1	20030731	DE 2002-10203346	20020129
WO 2003064652	A1	20030807	WO 2003-EP590	20030122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1472355	A1	20041103	EP 2003-734683	20030122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006088903	A1	20060427	US 2004-503253	20040729
			DE 2002-10203346 A	20020129
PRIORITY APPLN. INFO.:			WO 2003-EP590 W	20030122

AB A method for increasing the yield of zymosterol or its metabolites (anabolic or catabolic) in a transgenic microorganism is described. The yield is increased by increasing the levels of lanosterol demethylase and HMG CoA reductase activity in the cell. Overexpression of a gene for a truncated HMG CoA reductase in Saccharomyces cerevisiae using the promoter of the ADH alc. dehydrogenase gene resulted in a 90-fold increase in squalene yields. Yields of several sterols were increased by 20-250%. The yield of ergosterol was not affected. Addnl. overexpression of the ERG1 lanosterol demethylase gene using the same promoter increased the yield of ergosterol and lowered yields of squalene and lanosterol.

L4 ANSWER 10 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2003:86017 CAPLUS
DOCUMENT NUMBER: 138:334167
TITLE: Steroid biosynthesis in prokaryotes: identification of myxobacterial steroids and cloning of the first bacterial 2,3(S)-oxidosqualene cyclase from the myxobacterium Stigmatella aurantiaca
AUTHOR(S): Bode, Helge Bjorn; Zeggel, Bernd; Silakowski, Barbara; Wenzel, Silke C.; Reichenbach, Hans; Muller, Rolf
CORPORATE SOURCE: GBF - Gesellschaft fur Biotechnologische Forschung, Abteilung NBI/MX, Braunschweig, 38124, Germany
SOURCE: Molecular Microbiology (2003), 47(2), 471-481
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Steroids, such as cholesterol, are synthesized in almost all eukaryotic cells, which use these triterpenoid lipids to control the fluidity and flexibility of their cell membranes. Bacteria rarely synthesize such

tetracyclic compds. but frequently replace them with a different class of triterpenoids, the pentacyclic hopanoids. The intriguing mechanisms involved in triterpene biosynthesis have attracted much attention, resulting in extensive studies of squalenehopene cyclase in bacteria and (S)-2,3-oxidosqualene cyclases in eukarya. Nevertheless, almost nothing is known about steroid biosynthesis in bacteria. Only three steroid-synthesizing bacterial species have been identified before this study. Here, we report on a variety of sterol-producing myxobacteria. Stigmatella aurantiaca is shown to produce cycloartenol, the well-known first cyclization product of steroid biosynthesis in plants and algae. Addnl., we describe the cloning of the first bacterial steroid biosynthesis gene, cas, encoding the cycloartenol synthase (Cas) of S. aurantiaca. Mutants of cas generated via sitedirected mutagenesis do not produce the compd. They show neither growth retardation in comparison with wild type nor any increase in ethanol sensitivity. The protein encoded by cas is most similar to the Cas proteins from several plant species, indicating a close evolutionary relationship between myxobacterial and eukaryotic steroid biosynthesis.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2003:564702 CAPLUS
DOCUMENT NUMBER: 139:334671
TITLE: Enzymological properties of sterol-C4-methyl-oxidase of yeast sterol biosynthesis
AUTHOR(S): Darnet, Sylvain; Rahier, Alain
CORPORATE SOURCE: Institut de Biologie Moleculaire des Plantes, Institut de Botanique, Centre National de la Recherche Scientifique, UPR-CNRS 2357, Strasbourg, 67083, Fr.
SOURCE: Biochimica et Biophysica Acta, Molecular and Cell Biology of Lipids (2003), 1633(2), 106-117
CODEN: BBMLPG; ISSN: 1388-1981
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Despite genes of the sterol methyl-oxidase component (SMO) of the sterol-C4-demethylation multienzymic complex have been identified in a variety of organisms and the key role played by SMO in yeast sterol biosynthesis, the enzymol. properties of yeast SMO have not been investigated. An enzymic assay for measuring specifically sterol 4α-methyl-oxidase activity in Saccharomyces cerevisiae has been developed for the first time by using [14C]-4,4-dimethyl-zymosterol as substrate. It allowed enzymically formed C4 mono- and di-demethylated products to be characterized as well as two novel C4-hydroxymethyl-zymosterol derivs. to be identified as immediate oxidative metabolites by the yeast 4,4-dimethyl-zymosterol 4α-methyl-oxidase (ScSMO). The properties of microsomal ScSMO have been established with respect to cofactor requirements and kinetics and the substrate selectivity examd. with a no. of 4,4-dimethyl- and 4α-methyl-sterols. Remarkably, ScSMO showed very low activity with 24-methylene-24-dihydrocycloartenol, the natural substrate of maize 4,4-dimethyl-sterol-C4-methyl-oxidase. Conversely, maize sterol-C4-methyl-oxidases showed extremely reduced activity with the natural substrate of ScSMO. The previously described antifungal agent, 6-amino-2-n-pentylbenzothiazole was shown to directly inhibit the microsomal ScSMO activity in vitro. The yeast system was more than 500 times more sensitive to this deriv. than the maize systems. These distinct substrate specificities and inhibitor sensitivities between yeast and plant sterol-4α-methyl-oxidases probably reflect diversity in the structure of their active sites in relation to the distinct sterol biosynthetic pathways.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2003:147375 CAPLUS
DOCUMENT NUMBER: 139:273370
TITLE: Evidence for multiple sterol methyl transferase pathways in Pneumocystis carinii
AUTHOR(S): Zhou, Wenxu; Nguyen, Thi Thuy Minh; Collins, Margaret

S.; Cushion, Melanie T.; Nes, W. David
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, TX, 79409-1061, USA
SOURCE: Lipids (2002), 37(12), 1177-1186
CODEN: LPDSAP; ISSN: 0024-4201
PUBLISHER: AOCS Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The sterol compn. of Pneumocystis carinii, an opportunistic pathogen responsible for life-threatening pneumonia in immunocompromised patients, was detd. Our purpose was to identify pathway-specific enzymes to impair using sterol biosynthesis inhibitors. Prior to this study, cholesterol (ca. 80% of total sterols), lanosterol, and several phytosterols common to plants (sitosterol and campesterol) were demonstrated in the fungus. In this investigation, we isolated all the previous sterols and many new compds. from P. carinii by culturing the microorganism in steroid-immunosuppressed rats. Thirty-one sterols were identified from the fungus (total sterol = 100 fg/cell), and seven sterols were identified from rat chow. Unusual sterols in the fungus not present in the diet included, 24(28)-methylenelanosterol, 24(28)E-ethylidene lanosterol, 24(28)Z-ethylidene lanosterol, 24β-ethyllanosta-25(27)-dienol, 24β-ethylcholest-7-enol, 24β-ethylcholesterol, 24β-ethylcholesta-5,25(27)-dienol, 24-methyllanosta-7-enol, 24-methyldesmosterol, 24(28)-methylenecholest-7-enol, 24β-methylcholest-7-enol, and 24β-methylcholesterol. The structural relationship of the 24-alkyl groups in the sterol side chain were demonstrated chromatog. relative to authentic specimens, by MS and high-resoln. 1H NMR. The hypothetical order of these compds. poses multiple phytosterol pathways that diverge from a common intermediate to generate 24β-Me or 24β-Et sterols. Formation of 24(28)E-Ethylidene lanosterol is considered to form an interrupted sterol pathway. Taken together, operation of distinct sterol methyltransferase (SMT) pathways that generate 24β-alkyl sterols in P. carinii with no counterpart in human biochem. suggests a close taxonomic affinity with fungi and provides a basis for mechanism-based inactivation of SMT enzyme to treat Pneumocystis pneumonia.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2002:85835 CAPLUS
DOCUMENT NUMBER: 136:213452
TITLE: Sterol and fatty acid composition of Candida lusitaniae clinical isolates
AUTHOR(S): Peyron, P.; Favel, A.; Calaf, R.; Michel-Nguyen, A.; Bonaly, R.; Coulon, J.
CORPORATE SOURCE: Lab. de Botan, Cryptogamie et Bil. Cellulaire, Faculte de Pharmacie, Marseille, 13385, Fr.
SOURCE: Antimicrobial Agents and Chemotherapy (2002), 46(2), 531-533
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The sterol and fatty acid compns. of four amphotericin B-resistant and of two amphotericin B-susceptible Candida lusitaniae clin. isolates were detd. A flow cytofluorometric susceptibility test (FCST) with a membrane potential-sensitive cationic dye was used as a complement to the conventional method for selecting the isolates. Compared to susceptible isolates, resistant ones showed a greatly reduced ergosterol content and changes in sterol compn., consistent with a defect in Δ8→7 isomerase. Within each group, no correlation between the sterol or fatty acid pattern or compn. and both the degree of in vitro susceptibility and FCST MIC was found.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 40 BIOTECHNO COPYRIGHT 2007 Elsevier Science B.V.
Full Text
on STN DUPLICATE
ACCESSION NUMBER: 2001:37385182 BIOTECHNO

TITLE: The Effect of the erg26-1 Mutation on the Regulation of Lipid Metabolism in Saccharomyces cerevisiae
AUTHOR: Baudry K.; Swain E.; Rahier A.; Germann M.; Batta A.; Rondet S.; Mandala S.; Henry K.; Tint G.S.; Edlind T.; Kurtz M.; Nickels Jr. J.T.
CORPORATE SOURCE: J.T. Nickels Jr., 245 N. 15th St., Philadelphia, PA 19102, United States.
E-mail: Joseph.Nickels@drexel.edu
SOURCE: Journal of Biological Chemistry, (20 APR 2001), 276/16 (12702-12711), 61 reference(s)
CODEN: JBCHA3 ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2001:37385182 BIOTECHNO
AB A temperature-sensitive Saccharomyces cerevisiae mutant harboring a lesion in the ERG26 gene has been isolated. ERG26 encodes 4α-carboxysterol-C3 dehydrogenase, one of three enzymatic activities required for the conversion of 4,4-dimethylzymosterol to zymosterol. Gas chromatography/mass spectrometry analyses of sterols in this mutant, designated erg26-1, revealed the aberrant accumulation of a 4-methyl-4-carboxy zymosterol intermediate, as well as a novel 4-carboxysterol. Neutral lipid radiolabeling studies showed that erg26-1 cells also harbored defects in the rate of biosynthesis and steady-state levels of mono-, di-, and triglycerides. Phospholipid radiolabeling studies showed defects in the rate of biosynthesis of both phosphatidic acid and phosphatidylinositol. Biochemical studies revealed that microsomes isolated from erg26-1 cells contained greatly reduced 4α-carboxysterol-C3 dehydrogenase activity when compared with microsomes from wild type cells. Previous studies have shown that loss of function mutations in either of the fatty acid elongase genes SUR4/ELO3 or FEN1/GNS1/ELO2 can "by-pass" the essentiality of certain ERG genes (Ladeveze, V., Marcireau, C., Delourme, D., and Karst, F. (1993) Lipids 28, 907-912; Silve, S., Leplatoie, P., Josse, A., Dupuy, P. H., Lanau, C., Kaghad, M., Dhers, C., Picard, C., Rahier, A., Taton, M., Le Pur, G., Caput, D., Ferrara, P., and Loison, G. (1996) Mol. Cell. Biol. 16, 2719-2727). Studies presented here have shown that this sphingolipid-dependent "bypass" mechanism did not suppress the essential requirement for zymosterol biosynthesis. However, studies aimed at understanding the underlying physiology behind the temperature-sensitive growth defect of erg26-1 cells showed that the addition of several antifungal compounds to the growth media of erg26-1 cells could suppress the temperature-sensitive growth defect. Fluorescence microscopic analysis showed that GFP-Erg26p and GFP-Erg27p fusion proteins were localized to the endoplasmic reticulum. Two-hybrid analysis indicated that Erg25p, Erg26p, and Erg27p, which are required for the biosynthesis of zymosterol, form a complex within the cell.

L4 ANSWER 15 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2001:126046 CAPLUS
DOCUMENT NUMBER: 134:323244
TITLE: A novel gene conserved from yeast to humans is involved in sterol biosynthesis
AUTHOR(S): Gachotte, D.; Eckstein, J.; Barbuch, R.; Hughes, T.; Roberts, C.; Bard, M.
CORPORATE SOURCE: Department of Biology, Indiana University-Purdue University Indianapolis, Indianapolis, IN, 46202, USA
SOURCE: Journal of Lipid Research (2001), 42(1), 150-154
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ERG28 gene was originally identified by microarray expression profiling as possibly involved in the Saccharomyces cerevisiae sterol pathway. Microarray analyses suggested that the transcription pattern of ERG28 closely followed that of genes involved in sterol synthesis. ERG28 was also found in Schizosaccharomyces pombe and Arabidopsis as well as humans, and in the latter was shown to be highly expressed in adult testis tissue. All four proteins contain potential transmembrane domain(s). Gas chromatog.-mass spectrometry anal. of an ERG28-deleted S. cerevisiae

strain (which is slow growing but not auxotrophic for ergosterol) indicates a lesion in sterol C-4 demethylation. Sterol profiles indicate accumulation of 3-keto and carboxylic acid sterol intermediates, which are involved in removing the two C-4 Me groups from the sterol A ring. Similar intermediates have previously been demonstrated to accumulate in erg26 (sterol dehydrogenase/decarboxylase) and erg27 (3-ketoreductase) mutants in yeast. We speculate that the role of the Erg28 protein (Erg28p) may be either to tether Erg26p and Erg27p to the endoplasmic reticulum or to facilitate interaction between these proteins.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text

ACCESSION NUMBER: 2000:628250 CAPLUS
DOCUMENT NUMBER: 133:188459
TITLE: Meiosis activating sterol augments implantation rate
INVENTOR(S): Andersen, Claus Yding; Byskov, Anne Grete
PATENT ASSIGNEE(S): Den.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000052142	A2	20000908	WO 2000-DK80	20000225
WO 2000052142	A3	20010322		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2365225	A1	20000908	CA 2000-2365225	20000225
BR 2000008536	A	20011106	BR 2000-8536	20000225
EP 1157096	A2	20011128	EP 2000-904869	20000225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
HU 200200201	A2	20020529	HU 2002-201	20000225
JP 2002537801	T	20021112	JP 2000-602754	20000225
ZA 2001006101	A	20020204	ZA 2001-6101	20010725
US 2002042927	A1	20020411	US 2001-929800	20010814
NO 2001004120	A	20011025	NO 2001-4120	20010824
US 2005175976	A1	20050811	US 2003-626053	20030724
PRIORITY APPLN. INFO.:			DK 1999-273 A	19990226
			WO 2000-DK80 W	20000225
			US 2001-929800 B1	20010814

AB The present invention relates to the use of a new principle for improving the viability and pregnancy potential of oocytes and pre-embryos obtained in connection with in vitro fertilization and pre-embryo transfer treatment. More specifically, improvement by raising the content of Meiosis Activating Sterols (MAS) in the medium where the in vitro fertilization takes place. This is achieved by exposing and culturing one or more oocytes with spermatozoa in a culture medium comprising at least one meiosis activating sterol (MAS), a MAS analog, and/or an additive or additives capable of endogenous stimulation of the accumulation of at least one MAS. Preferred additives are FSH and EGF.

L4 ANSWER 17 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text

ACCESSION NUMBER: 1999:234007 CAPLUS
DOCUMENT NUMBER: 130:280919
TITLE: Method for producing ergosterol and intermediates by recombinant yeast fermentation
INVENTOR(S): Weber, Alfred; Klages, Uwe; Kennecke, Mario; Lang, Christine; Stahl, Ulf; Polakowski, Thomas
PATENT ASSIGNEE(S): Schering A.-G., Germany

SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9916886	A1	19990408	WO 1998-EP6134	19980928
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19744212	A1	19990415	DE 1997-19744212	19970930
DE 19744212	B4	20060119		
CA 2305780	A1	19990408	CA 1998-2305780	19980928
AU 9911474	A	19990423	AU 1999-11474	19980928
AU 750768	B2	20020725		
EP 1015597	A1	20000705	EP 1998-954286	19980928
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
HU 200003751	A2	20010228	HU 2000-3751	19980928
JP 2001518301	T	20011016	JP 2000-513955	19980928
RU 2235777	C2	20040910	RU 2000-109974	19980928
NO 2000001625	A	20000329	NO 2000-1625	20000329
US 2004235088	A1	20041125	US 2003-665649	20030922
PRIORITY APPLN. INFO.:			DE 1997-19744212 A	19970930
			WO 1998-EP6134 W	19980928
			US 2000-509608 B1	20000619

AB The invention concerns the prodn. of ergosterol in yeast by constructing plasmids with the ergosterol biosynthesis genes; transformation, expression of the genes in yeast cells, fermn.; and isolation of ergosterol and its intermediates in chromatog. columns. Plasmids are constructed contg. single genes or their combination. The following genes are involved: t-HMG, coding for HMG-Co-A-Reductase; ERG9, coding for squalene synthetase; SAT1, coding for Acyl-CoA:Sterol-acetyltransferase; and ERG1, coding for squalene epoxidase. A DNA sequence coding for tHMG was amplified from genomic DNA of Saccharomyces cerevisiae using tHMG-5' and tHMG-3' primers. The DNA fragment was inserted into the pUC19 cloning vector; the pUC19-tHMG plasmid was isolated, ligated with yeast expression vector pPT2b. The obtained pPT2b-tHMG vector contained the ADH1 promoter, the tHMG fragment and the TRP1 terminator; it was cleaved at the EcoRV and NruI site; the fragment contg. the middle part of ADH1, tHMG and TRP1 terminator was inserted into in the YEp13 yeast vector. The resulting YEpH2 vector included the tetracycline resistance gene, the middle part of the ADH1 promoter, the tHMG and the TRP1 terminator; it was inserted into the YDpU vector resulting YDpUH2/12; ligated to the kanamycin resistance gene; the result was the YDpUHK3 construct. The S. cerevisiae AH22 strain was transformed with the construct; resulting in an integration at the URA3 gene locus. Transformed yeast cells underwent FOA selection; the uracil auxotrophic strain AH22/tH3ura8 was isolated that contained the tHMG1 expression cassette in chromosomal integration at the URA3 gene. Fermn. of the transformed yeast resulted increased HMG-CoA-reductase activity; increased squalene and ergosterol prodn. compared to the non-transformed AH22 cells. Similar procedure resulted the transformed AH22/pADL-SAT1 yeast cells that contained the SAT1 gene in the pADL-SAt1 expression vector. Fermn. of the AH22/pADL-SAT1 resulted in no squalene and increased ergosterol compared to the non-transformed strain. The pADL-SAt1 expression vector was inserted into transformed AH22/tH3ura8 cells; the resulting AH22/tH3ura8/pADL-SAT1 yeast cells produced 5.540 wt./wt.% ergosterol compared with 3.798 wt./wt.% produced by the AH22/tH3ura8 (expressed in % of yeast dry mass). The optimum uracil concn. in the culture medium was 20 µg/mL. Varying the culture media compn., the concn. of the intermediates changes; thus different concns. of lanosterol, 4,4-dimethylzymosterol, zymosterol, ergost-7-enol, and ergosta-5,7-dienol were obtained. The AH22/tH3ura8/pADL-SAT1 strains produced mainly lanosterol and 4,4-dimethylzymosterol as intermediates.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text

ACCESSION NUMBER: 1996:155587 CAPLUS
DOCUMENT NUMBER: 124:202733
TITLE: Sterol derivatives used for regulation of meiosis
INVENTOR(S): Byskov, Anne Grete; Andersen, Claus Yding; Nordholm, Lars; Thoegersen, Henning; Wassmann, Ole; Diers, Ivan Verner; Guddal, Erling
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9600235	A1	19960104	WO 1995-DK265	19950623
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TT, UA, UG, US, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2192941	A1	19960104	CA 1995-2192941	19950623
AU 9527343	A	19960119	AU 1995-27343	19950623
AU 694240	B2	19980716		
ZA 9505213	A	19960315	ZA 1995-5213	19950623
EP 767798	A1	19970416	EP 1995-922448	19950623
EP 767798	B1	20030903		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CN 1151164	A	19970604	CN 1995-193731	19950623
CN 1068333	B	20010711		
BR 9508074	A	19970812	BR 1995-8074	19950623
HU 76343	A2	19970828	HU 1996-3584	19950623
JP 10502060	T	19980224	JP 1995-502724	19950623
CZ 289407	B6	20020116	CZ 1996-3725	19950623
IL 114294	A	20020912	IL 1995-114294	19950623
RU 2194510	C2	20021220	RU 1997-101087	19950623
AT 248852	T	20030915	AT 1995-922448	19950623
PL 186688	B1	20040227	PL 1995-317830	19950623
ES 2204955	T3	20040501	ES 1995-922448	19950623
FI 9605144	A	19970220	FI 1996-5144	19961220
FI 117159	B1	20060714		
NO 9605516	A	19970221	NO 1996-5516	19961220
NO 314534	B1	20030407		
PRIORITY APPLN. INFO.:			DK 1994-753 A	19940623
			DK 1995-241 A	19950309
			WO 1995-DK265 W	19950623

OTHER SOURCE(S): MARPAT 124:202733
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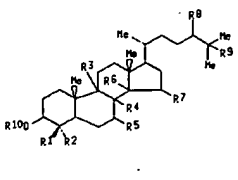


I

AB Steroids I [R1, R2 = H, (un)substituted alkyl; R1R2 = alkylene; R3R4, R4R5, R4R6, R6R7 = bond, the others = H; R8, R9 = H; R8R9 = bond; R10 = H, acyl, sulfonyl, phosphonyl] were prepd. or extd. from bull testes or human follicular fluid for use in stimulating meiosis. Thus, 4,4-dimethylcholesta-8,14-dien-3β-ol was converted to its benzoate, reduced with BH3, dehydrated and debenzoylated to give 4,4-dimethylcholest-8-en-3β-ol which showed meiosis-stimulating activity.

L4 ANSWER 19 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text

ACCESSION NUMBER: 1992:526051 CAPLUS
DOCUMENT NUMBER: 117:126051
TITLE: Combined action of a fluorescent brightening agent and polyoxyethylene alkylalcohol ether on yeast
AUTHOR(S): Sugihara, Toshiharu
CORPORATE SOURCE: Fac. Educ., Gifu Univ., Gifu, 501-11, Japan
SOURCE: Nippon Kasei Gakkaishi (1992), 43(3), 207-14
CODEN: NKGAEB; ISSN: 0913-5227
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The influence of the fluorescent brightener, di-Na 4,4'-bisphenylureidostilbene-2,2'-disulfonate (I), on Saccharomyces cerevisiae yeast was investigated in the presence of a series of polyoxyethylene alkyl ethers (POEs). The nonionic surfactants changed the action of I on the yeast depending on their nature. Hydrophobic surfactants with I decreased more the growth of the yeast and the rate of surviving cells after incubation than with I alone, which was accompanied by stronger inhibition of sterol biosynthesis and of enzymes related to the electron-transport process. Extracellular enzymes were greatly enhanced in the presence of hydrophobic surfactants and I. On the other hand, the surfactants with low hydrophobicity exhibited the opposite action in reducing the influence of I on the biol. processes in yeast. POEs had little effect on the growth. The effects of POE and I on the biochem. processes of yeast correlated well with the hydrophilic-lipophilic balance (HLB) of the surfactants. This phenomenon is interpreted in terms of the change in interaction of I in POE micelles with yeast, and is supported by data on adsorption isotherms of PBA to yeast in the presence of POE.

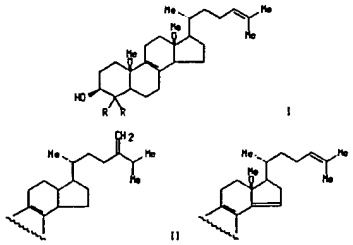
L4 ANSWER 20 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text

ACCESSION NUMBER: 1993:97890 CAPLUS
DOCUMENT NUMBER: 118:97890
TITLE: Ergosterol depletion and 4-methyl sterols accumulation in the yeast Saccharomyces cerevisiae treated with an antifungal, 4-amino-2-n-pentylthiobenzothiazole
AUTHOR(S): Kuchta, Tomas; Bartkova, Katrina; Kubinec, Robert
CORPORATE SOURCE: Food Res. Inst., Modra, CS-90001, Czech.
SOURCE: Biochemical and Biophysical Research Communications (1992), 189(1), 85-91
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In Saccharomyces cerevisiae treated with 6-amino-2-n-pentylthiobenzothiazole, levels of ergosterol and other 4-desmethylsterols were significantly reduced. Major sterols in treated yeast were lanosterol, 4,4-dimethylzymosterol, 4-methylzymosterol, and 4-methylfecosterol. A hypothesis that the antifungal agent inhibits sterol demethylation at C-4 and forces biosynthesis to a blind pathway ending in 4-methylfecosterol is presented.

L4 ANSWER 21 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text

ACCESSION NUMBER: 1989:39243 CAPLUS
DOCUMENT NUMBER: 110:39243
TITLE: Synthesis of zymosterol, fecosterol, and related biosynthetic sterol intermediates
AUTHOR(S): Dolle, Roland E.; Schmidt, Stanley J.; Erhard, Karl F.; Kruse, Lawrence I.
CORPORATE SOURCE: Dep. Med. Chem., Smith Kline and French Res. Ltd., The Frythe/Welwyn/Hertfordshire, AL6 9AR, UK

SOURCE: Journal of the American Chemical Society (1989), 111(1), 278-84
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 110:39243
GI



I

II

III

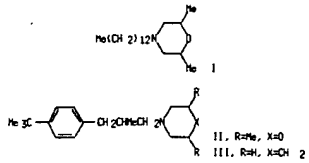
AB The prepns. of zymosterol (I, R = H), fecosterol (II, R = H), and related compds. I (R = Me) and III (R = H, Me) are described in detail.

L4 ANSWER 22 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1986:530460 CAPLUS
DOCUMENT NUMBER: 105:130460
TITLE: Dimorphism-associated variations in the lipid composition of Candida albicans
AUTHOR(S): Ghannoum, M. A.; Janini, G.; Khamis, L.; Radwan, S. S.
CORPORATE SOURCE: Dep. Bot. Microbiol., Kuwait Univ., Kuwait, Kuwait
SOURCE: Journal of General Microbiology (1986), 132(8), 2167-75
CODEN: JGMIAN; ISSN: 0022-1287
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Yeast and mycelial forms of C. albicans ATCC 10231, growing together in 12-h and in 96-h cultures, were sepd. and their lipids were extd. and characterized. The total lipid content of the yeast forms was always lower than that of the mycelial forms. In 12-h cultures the lipids from the 2 morphol. forms consisted mainly of polar compds., viz. phospholipids and glycolipids. In 96-h cultures both the yeast and mycelial forms accumulated substantial amts. of apolar compds., mainly steryl esters and triacylglycerols. The mycelial forms were more active than the yeast forms in this respect. Major differences in the lipid compn. between the 2 morphol. forms involved the contents of sterols and complex lipids that contain sterols. As a rule, the yeast lipids contained much larger proportions of free sterols than the mycelial lipids. However, the mycelial lipids contained several times more sterols than the yeast forms but bound as steryl glycosides, esterified steryl glycosides, and steryl esters. Steryl glycosides and esterified steryl glycosides occurred in yeast lipids only in traces, if at all. The major steryl glycoside in the mycelial forms was unequivocally identified as cholesteryl mannoside. At both phases of growth the apolar and polar lipid fractions from the mycelial forms contained higher levels of polyunsatd. fatty acids (18:2 and 18:3), but lower levels of oleic acid (18:1) than the corresponding fractions from the yeast forms. The lipid content and compn. of 12-h and 96-h yeast and mycelial forms of C. albicans KCCC 14172, a clin. isolate,

were almost identical with those of C. albicans ATCC 10231.

L4 ANSWER 23 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1986:587287 CAPLUS
DOCUMENT NUMBER: 105:187287
TITLE: Amphotericin B action on the sterol composition of Kluyveromyces bulgaricus and Kluyveromyces lactis
AUTHOR(S): Coulon, J.; Hakkou, A.; Mpona-Minga, M.; Bonaly, R.
CORPORATE SOURCE: Lab. Biochim. Microb., Fac. Sci. Pharm. Biol., Nancy, 54001, Fr.
SOURCE: Canadian Journal of Microbiology (1986), 32(9), 738-42
CODEN: CJMIAZ; ISSN: 0008-4166
DOCUMENT TYPE: Journal
LANGUAGE: French
AB The degree of sensitivity of the yeasts K. bulgaricus and K. lactis to amphotericin B is linked to a difference in the sterol compn. of their membranes. No direct proportionality was found between sensitivity and the quantity of sterols present. At sublethal doses, amphotericin B perturbed sterol synthesis, resulting in ergosterol precursor accumulation. An ergosterol pathway is proposed for Kluyveromyces.

L4 ANSWER 24 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1985:75530 CAPLUS
DOCUMENT NUMBER: 102:75530
TITLE: Inhibition of ergosterol biosynthesis in Saccharomyces cerevisiae and Ustilago maydis by tridemorph, fenpropimorph and fenpropidin
AUTHOR(S): Baloch, Roobina I.; Mercer, E. Ian; Wiggins, Thomas E.; Baldwin, Brian C.
CORPORATE SOURCE: Dep. Biochem. Agric. Biochem., Univ. Coll. Wales, Aberystwyth/Dyfed, SY23 3DD, UK
SOURCE: Phytochemistry (Elsevier) (1984), 23(10), 2219-26
CODEN: PYTCAS; ISSN: 0031-9422
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

II, R=Me, X=O
III, R=H, X=OH 2

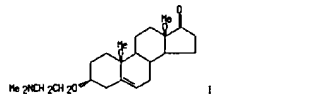
AB The structurally related fungicides tridemorph (I), fenpropimorph (II), and fenpropidine (III) inhibited sterol Δ14-reductase and Δ8 → Δ7-isomerase during ergosterol biosynthesis in Saccharomyces cerevisiae and Ustilago maydis. However, although the 3 fungicides inhibit both enzymes, I inhibits the Δ8-Δ7-isomerase better than Δ14-reductase while the reverse is true for III and to a lesser extent for II.

L4 ANSWER 25 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1985:500268 CAPLUS
DOCUMENT NUMBER: 103:100268
TITLE: Where do morpholines inhibit sterol biosynthesis?
AUTHOR(S): Baloch, R. I.; Mercer, E. I.; Wiggins, T. E.; Baldwin, B. C.
CORPORATE SOURCE: Dep. Biochem. Agric. Biochem., Univ. Coll. Wales,

Aberystwyth, SY23 3DD, UK
SOURCE: British Crop Protection Conference--Pests and Diseases, Proceedings (1984), (3), 893-8
CODEN: PBCDDQ; ISSN: 0144-1612
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Morpholine fungicides block both Δ3->Δ7-isomerization and the Δ14-redn. steps during ergosterol biosynthesis in fungi, as shown by studies in Saccharomyces cerevisiae and Ustilago maydis, using tridemorph [81412-43-3], fenpropimorph [67306-03-0] and fenpropidin [67306-00-7]. However, tridemorph inhibits the Δ3->Δ7-isomerase better than the Δ14-reductase, whilst the reverse is true for fenpropidin and to a lesser extent for fenpropimorph.

L4 ANSWER 26 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1981:26895 CAPLUS
DOCUMENT NUMBER: 94:26895
TITLE: The separation of sterol intermediates in cholesterol biosynthesis by high pressure liquid chromatography
AUTHOR(S): Hansbury, Elizabeth; Scallen, Terence J.
CORPORATE SOURCE: Sch. Med., Univ. New Mexico, Albuquerque, NM, 87131, USA
SOURCE: Journal of Lipid Research (1980), 21(7), 921-9
CODEN: JLPRAW; ISSN: 0022-2275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A 3-step procedure was applied to the sepn. of sterol intermediates formed from [14C]mevalonate by normal rat hepatocyte culture cells. In step (1) a short gravity-flow silicic acid column (1.2 × 6.5 cm) seps. the incubation products into 4 classes consisting of (A) squalene + squalene oxide, (B) Me sterol precursors, (C) C27 sterols, and (D) polar compds. In step (2), the components of classes (B) and (C) are further resolved by reverse-phase high-pressure liq. chromatog. (reverse-phase HPLC) on a μBondapak-C18 column. In step (3), (after acetylation), HPLC on a μPorasil column of peaks obtained from Step (2) is conducted. Step 3 resolves mixts. which may be present in peaks resulting from step (2). Relative retention time (RRT) factors for several functional groups encountered in sterol intermediates in cholesterol biosynthesis were detd. for both reverse-phase and silicic acid HPLC systems. Use of these functional group factors allows the calcn. of a predicted RRT for a variety of structural possibilities. The HPLC techniques utilize single columns, isocratic solvent systems, comparatively short (<30 min) elution times, and the 3-step procedure is capable of resolving complex mixts. of sterol intermediates.

L4 ANSWER 27 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1979:534758 CAPLUS
DOCUMENT NUMBER: 91:134758
TITLE: The effects of the hypocholesteremic compound 3β-(β-dimethylaminoethoxy)-androst-5-en-17-one on the sterol and steryl ester composition of Saccharomyces cerevisiae
AUTHOR(S): Field, Ruth B.; Holmlund, Chester E.; Whittaker, Noel F.
CORPORATE SOURCE: Dep. Chem., Univ. Maryland, College Park, MD, 20742, USA
SOURCE: Lipids (1979), 14(8), 741-7
CODEN: LPDSAP; ISSN: 0024-4201
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB When yeast was grown in the presence of 10-4M 3β-(β-dimethylaminoethoxy)androst-5-en-17-one (I) [7635-03-2], 2,3;22,23-dioxidosqualene [31063-19-1] accumulated. Total free sterol was reduced by ~30%, whereas almost no steryl esters were found. The same drug at lower concn. (3 × 10-6M) caused a slight increase in steryl ester prodn., and a 24% redn. in free sterol content. The marked accumulation of ergosta-5,7,22,24(28)-tetraen-3β-ol [7720-30-1] with 3 × 10-6M I indicated that the C24-28 reductase is esp. sensitive to the action of the drug.

L4 ANSWER 28 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1979:402273 CAPLUS
DOCUMENT NUMBER: 91:2273
TITLE: Azasterol inhibitors in yeast. Inhibition of the Δ24-sterol methyltransferase and the 24-methylene sterol Δ24(28)-reductase in sterol mutants of Saccharomyces cerevisiae
AUTHOR(S): Pierce, A. M.; Unrau, A. M.; Oehlschlager, A. C.; Woods, R. A.
CORPORATE SOURCE: Dep. Chem., Simon Fraser Univ., Burnaby, BC, V5A 1S6, Can.
SOURCE: Canadian Journal of Biochemistry (1979), 57(3), 201-8
CODEN: CJBIAE; ISSN: 0008-4018
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of several nonoxasterols on sterol biosynthesis were examd. in the ergosterol-deficient mutants erg2, erg3, and erg5 of S. cerevisiae. When the mutants were aerobically cultured in the presence of 1 μM 23-azacholesterol, the 24-methylene sterol Δ24(28)-reductase was essentially blocked and the immediate Δ24(28)-unsatd. precursor of the final sterol metabolite in each resp. erg strain was found to accumulate. Total sterol prodn. was enhanced in the cultures grown in the presence of 1 μM 23-azacholesterol. In cultures which were grown in the presence of 1 μM 25-azacholesterol, which effectively blocked the Δ24-sterol methyltransferase, all 3 erg strains accumulated zymosterol as the major sterol component with lesser quantities of predicted terminal sterols. Mutant erg2 (block at Δ8→Δ7 isomerase) grew poorly in the presence of 1 μM 25-azacholesterol and produced low levels of cholesta-5,8,24-trienol and cholesta-5,8,22,24-tetraenol, which were isolated and characterized. Compared with controls, erg2 treated with 1 μM 23-azacholesterol produced increased amts. of ergosta-5,8,22,24(28)-tetraenol, which was hitherto unidentified as a yeast sterol. In erg5 (block at Δ22-dehydrogenase) treatment with 1 μM 25-azacholestanol effectively blocked the Δ24-sterol methyltransferase and resulted in increased total sterol prodn. Cholesta-5,7,24-trienol accounted for 27-9% of the sterol pool in 25-azasterol inhibited erg5 cultures. The 25-azasterol-inhibited erg5 mutant thus provides a source of cholesta-5,7,24-trienol, a potential provitamin D3 substitute.

L4 ANSWER 29 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1979:146104 CAPLUS
DOCUMENT NUMBER: 90:146104
TITLE: Effect of hypocholesterolemic agents on central nervous system cholesterol biosynthesis. III. Zuclomiphene in combination with AY9944 and Triparanol
AUTHOR(S): Ramsey, Robert B.
CORPORATE SOURCE: Dep. Neurol., St. Louis Univ. Sch. Med., St. Louis, MS, USA
SOURCE: Biochemical Pharmacology (1978), 27(12), 1637-40

CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
AB AY 9944-Triparanol-zuclomiphene mixt. (I) [69762-37-4] (3:30:30 mg/kg, i.p., twice weekly from day 4 to 20 of age, totalling 5 injections) caused an accumulation in cholesterol [57-88-5]-precursor sterols, particularly those with Δ5,7 double bonds, in the brains of developing rats. After I, the squalene oxide [7200-26-2] and steryl ester fraction contained more label from an intracerebral injection of mevalonic acid-2-14C, whereas there was less label in cholesterol, and in the squalene [111-02-4], free sterol, and digitonide-precipitable sterol fractions label content was unchanged. I increased labeled zymosterol [128-33-6] but decreased labeled desmosterol [313-04-2] in the brain. I produced overall increases in brain labeled C-4 Me sterols.

L4 ANSWER 30 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1978:500829 CAPLUS
DOCUMENT NUMBER: 89:100829
TITLE: Azasterol inhibitors in yeast. Inhibition of the 24-methylene sterol Δ24(28)-reductase and Δ24-sterol methyltransferase of Saccharomyces cerevisiae by 23-azacholesterol
AUTHOR(S): Pierce, H. D., Jr.; Pierce, A. M.; Srinivasan, R.; Unrau, A. M.; Oehlschlager, A. C.
CORPORATE SOURCE: Dep. Chem., Simon Fraser Univ., Burnaby, BC, Can.
SOURCE: Biochimica et Biophysica Acta, Lipids and Lipid Metabolism (1978), 529(3), 429-37
CODEN: BBLLA6; ISSN: 0005-2760
DOCUMENT TYPE: Journal
LANGUAGE: English
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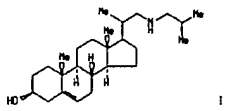


I

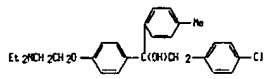
AB The effects of 23-azacholesterol (I) [29588-39-4] on sterol biosynthesis and growth of S. cervisiae were exam. In the presence of 0.2, 0.5, and 1 μM I, aerobically-growing yeast produced a nearly const. amt. of ergosta-5,7,22,24(28)-tetraen-3β-ol [7720-30-1] (~36% of total sterol) and slowly accumulated zymosterol [128-33-6] with a concomitant decline in ergosterol [57-87-4] synthesis. Growth and total sterol content of yeast cultures treated with 0.2-1 μM I were similar to that of the control culture. Yeast cultures treated with 5 and 10 μM I produced mostly zymosterol (58-61% of total sterol), whereas ergosta-5,7,22,24(28)-tetraenol prodn. declined to <10% of total sterol. The obsd. changes in the distribution of sterols in treated cultures are consistent with inhibition of 24-methylene sterol 24(28)-reductase [56467-82-4] (total inhibition at 1 μM I) and of Δ24-sterol methyltransferase [37257-07-1] (71% inhibition at 10 μM I). Yeast cultures treated with 10 μM I contained 4,4-dimethyl-5α-cholesta-8,14,24-trien-3β-ol [64284-64-6] and 4α-methyl-5α-cholesta-8,14,24-trien-3β-ol [67445-13-0], which were isolated and characterized for the first time.

L4 ANSWER 31 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1978:419944 CAPLUS
DOCUMENT NUMBER: 89:19944
TITLE: Sterol biosynthesis by strains of Saccharomyces cerevisiae in the presence and absence of dissolved oxygen
AUTHOR(S): Aries, Vivienne; Kirsop, B. H.

CORPORATE SOURCE: Brew. Res. Found., Nutfield/Redhill/Surrey, UK
SOURCE: Journal of the Institute of Brewing (1978), 84(2), 118-22
CODEN: JINBAL; ISSN: 0368-2587
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The content of sterols in S. cerevisiae which has been harvested after anaerobic growth and then added to a complex nutrient medium, rises rapidly from ca. 1 mg/g dry yeast to ca. 10 mg in the presence of dissolved O. A range of sterols, present principally as sterol esters, is formed during this period. The concn. of free sterols does not rise above 3 mg/g and esters are thought to form a reserve sterol pool. Cyclization of squalene to lanosterol [79-63-0] in the presence of O seems not to be markedly affected by O concn. in contrast to demethylation and desatn. reactions on the pathway to ergosterol [57-87-4]. When O concn. falls to zero, further metab. of preformed sterols continues, with the accumulation of episterol [474-68-0] and ergosterol and redn. in the concn. of zymosterol [128-33-6] and 24(28)-dehydroergosterol [7720-30-1]. During anaerobic growth a marked hydrolysis of sterol esters occurs and free sterols eventually predominate.

L4 ANSWER 32 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1979:50484 CAPLUS
DOCUMENT NUMBER: 90:50484
TITLE: Involvement of cytochrome P-450 and a cyanide-sensitive enzyme in different steps of lanosterol demethylation by yeast microsomes
AUTHOR(S): Ohba, Masayuki; Sato, Ryo; Yoshida, Yuzo; Nishino, Tokuzo; Katsuki, Hirohiko
CORPORATE SOURCE: Inst. Protein Res., Osaka Univ., Suita, Japan
SOURCE: Biochemical and Biophysical Research Communications (1978), 85(1), 21-7
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the presence of NADPH, NAD, and O2, microsomes prepd. from Saccharomyces cerevisiae converted lanosterol-1,7,15,22, 26,30-14C to 4,4-dimethylzymosterol, 4-methylzymosterol, and zymosterol. This conversion was accompanied by the liberation of 14CO2 derived from the Me group (C-30) at the 4-position. 14CO2 formation was inhibited by antibodies to yeast cytochrome P 450 and by CN-. Gas chromatog. indicated that the antibodies inhibited the conversion of lanosterol to 4,4-dimethylzymosterol, whereas the demethylation of the latter to 4-methylzymosterol was sensitive to CN-. Thus, cytochrome P 450 and a CN--sensitive enzyme are involved in the CN--sensitive enzyme are involved in the 14α- and 4-demethylations of lanosterol, resp., by yeast microsomes.

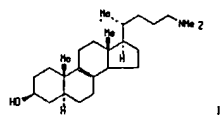
L4 ANSWER 33 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1978:69663 CAPLUS
DOCUMENT NUMBER: 88:69663
TITLE: The effect of triparanol on the composition of free and esterified sterols of Saccharomyces cerevisiae
AUTHOR(S): Campagnoni, Celia; Holmlund, Chester E.; Whittaker, Noel
CORPORATE SOURCE: Dep. Chem., Univ. Maryland, College Park, MD, USA
SOURCE: Archives of Biochemistry and Biophysics (1977), 184(2), 555-60
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Triparanol (I) [78-41-1] altered the sterol compn. of S. cerevisiae and promoted an increase in the steryl ester and total sterol per organism. The accumulation of Δ8-sterols, both free and esterified, in the presence of I indicated that a major effect of the compd. in yeast is the inhibition of the Δ8→7 isomerase. Isolation of ergosta-5,8(9),22-trien-3β-ol [50657-31-3], hitherto detected only in ergosterol-deficient yeast mutants, further supports the concept that all of the other metabolic alterations required for the conversion of lanosterol to ergosterol can occur without the necessity of Δ8→7 isomerization.

L4 ANSWER 34 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1976:489923 CAPLUS
DOCUMENT NUMBER: 85:89923
TITLE: The induced biosynthesis of 7-dehydrocholesterols in yeast: potential sources of new provitamin D3 analogs
AUTHOR(S): Avruch, L.; Fischer, S.; Pierce, H., Jr.; Oehlschlager, A. C.
CORPORATE SOURCE: Dep. Chem., Simon Fraser Univ., Burnaby, BC, Can.
SOURCE: Canadian Journal of Biochemistry (1976), 54(7), 657-65
CODEN: CJBIAE; ISSN: 0008-4018
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The effect of low concns. of a specifically designed sterol-24-transmethylase inhibitor, 25-aza-24,25-dihydrozymosterol (I) on sterol prodn. in Saccharomyces cerevisiae was exam. The synthesis of cholesta-5,7,22,24-tetraen-3β-ol, its 7,22,24 analog, and the 7,24 analog coupled with the availability of zymosterol and cholesta-5,7,24-3β-ol derivs. facilitated a search for these sterols in cultures treated with this inhibitor. When S. cerevisiae was grown in the presence of 1.3 and 5 μM I, it produced no ergosterol but accumulated zymosterol, cholesta-5,7,22,24-tetraen-3β-ol, and related C27 sterols. These results indicate blockage of the side chain methylation that normally occurs during the biosynthesis of ergosterol in yeast by compd. I is efficient. The cholesta-5,7,22,24-tetraen-3β-ol is a close structural analog of provitamin D3 (7-dehydrocholesterol). The inhibited yeast thus provides a source of a potentially new provitamin D3 substitute.

L4 ANSWER 35 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1975:590211 CAPLUS
DOCUMENT NUMBER: 83:190211
TITLE: Nuclear demethylation and C-24 alkylation during ergosterol biosynthesis in Saccharomyces cerevisiae
AUTHOR(S): Fryberg, M.; Avruch, L.; Oehlschlager, A. C.; Unrau, A. M.

CORPORATE SOURCE: Dep. Chem., Simon Fraser Univ., Burnaby, BC, Can.
SOURCE: Canadian Journal of Biochemistry (1975), 53(8), 881-9
CODEN: CJBIAE; ISSN: 0008-4018
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of 4,4-dimethylzymosterol (I), 4,4-dimethylfecosterol (II) and 31-norlanosterol (III) in the biosynthesis of ergosterol (IV) in S. cerevisiae has been investigated. The synthesis of II and III coupled with the availability of I facilitated a search for these sterols in com. yeast sterol concns. Fresh lab.-grown yeast and fresh brewery grown yeast. II was not detected in any of these mixts. whereas III was found in the 1st and last and I was present in all 3 sources investigated. Investigation of incorporation of lanosterol-2-3H into I, II, and III revealed significant incorporation into I but neither II nor III. This observation suggests the principle pathway for ergosterol biosynthesis initially involved lanosterol → I → 4α-methylzymosterol (V). Incubation of a mixt. of zymosterol-2,4-3H and lanosterol-26,27-14C with S. cerevisiae revealed that during the initial phases of aerobic growth the major route from V to IV involves zymosterol VI but as VI accumulates 4α-methyl-24-methylenezymosterol assumes equal importance.

L4 ANSWER 36 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1970:506548 CAPLUS
DOCUMENT NUMBER: 73:106548
TITLE: S-adenosylmethionine: Δ24-sterol methyltransferase in ergosterol biosynthesis in yeast. Specificity of sterol substrates and inhibitors
AUTHOR(S): Moore, J. Thomas, Jr.; Gaylor, James L.
CORPORATE SOURCE: Grad. Sch. of Nutr., Cornell Univ., Ithaca, NY, USA
SOURCE: Journal of Biological Chemistry (1970), 245(18), 4684-8
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of an S-adenosylmethionine:Δ24-sterol methyltransferase (methyltransferase) in ergosterol biosynthesis in yeast has been investigated. Sterol substrate specificity studies indicate that zymosterol is the best Me group acceptor in the methyltransferase assay. 4-Me sterols are very poor substrates; sterols with a fully reduced side chain (i.e. no double bond at C-26) are not methylated. A corresponding 3-ketosteroid, 5α-cholesta-8,24-dien-3-one, was methylated at a slower rate; similarly, sterols with nuclear double bonds in positions 5 or 5 and 7 were poorer substrates than zymosterol. Inhibition studies indicate that sterols with a satd. isooctyl side chain are competitive inhibitors of zymosterol in the methyltransferase reaction. Sterols that possess an alkylated side chain markedly altered the rate of methyltransfer; at low concns. of substrate, addn. of 24-alkyl-substituted sterols stimulated the methyltransferase, whereas at higher concns. of substrate the 24-alkyl sterols were inhibitory.

L4 ANSWER 37 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1972:550053 CAPLUS
DOCUMENT NUMBER: 77:150053
TITLE: Sterol precursors of cholesterol in normal and tumor tissues
AUTHOR(S): Galli, G.; Galli-Kienle, M.; Cattabeni, F.; Fiecchi, A.; Grossi-Paoletti, E.; Paoletti, R.
CORPORATE SOURCE: Univ. Milan, Mialn, Italy
SOURCE: Advances in Enzyme Regulation (1970), 8, 311-21
CODEN: AEZRA2; ISSN: 0065-2571
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sterol compn. in human brain and brain tumors was detd. using combined chromatog. techniques. The identification of a Δ14-sterol in a normal brain opened the way to reappraisal of some of the mechanisms of the latest steps of cholesterol biosynthesis in mammalian tissues. The loss of the 15α-hydrogen of lanosterol is described, and the presence of a new series of cholesterol precursors (sterols contg. a 8,14-diene system) is demonstrated.

L4 ANSWER 38 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1970:1319 CAPLUS
DOCUMENT NUMBER: 72:1319
TITLE: Use of specific inhibitors for the selective investigation of sterol biosynthesis in mammalian tissues
AUTHOR(S): Galli, Giovanni; Fumagalli, R.; Grossi-Paoletti, Enrica; Paoletti, R.
CORPORATE SOURCE: Univ. Milan, Milan, Italy
SOURCE: Int. Conf. Radioactive Isotop. Pharmacol. (1969), Meeting Date 1967, 279-94. Editor(s): Waser, P. G. Wiley-Interasci.: London, Engl.
CODEN: 21TKAS
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Animals received 10% glucose soln. ad libitum for 16 hr before sacrifice a nd mevalonate-2-14C (200 μCi/kg) was injected in the femoral vein 1 hr before sacrifice. The rats were killed by decapitation. The livers excised and pooled. The sterols were isolated as acetates and identified by gas chromatog., ir spectra, and gas chromatog.-mass spectrometry. All sterol fractions were analyzed for radioactivity. The following sterols were identified and the percentage of the total ster ols detd.: cholesterol, 53.08%; desmosterol, 42.01%; zymosterol, 1.95%; C27 Δ7,24 st erol, 1.39%; zymostenol, 0.44%; 14-desmethyllanosterol, 0.22%; C28 Δ8,24 sterol, 0.15%; lathosterol, 0.12%; cholestanol, 0.11%; and unidentified sterols, 0.53%. By using selective inhibitors of cholesterol biosynthesis, such as triparanol, combined with radioactive substrates, it is possible to obtain considerable nos. of labeled precursors which are usually difficult to obtain chem.

L4 ANSWER 39 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1968:433989 CAPLUS
DOCUMENT NUMBER: 69:33989
TITLE: Sterols with 29, 28, and 27 carbon atoms, metabolically related to cholesterol, and occurring in developing and mature brain
AUTHOR(S): Weiss, J. F.; Galli, G.; Grossi-Paoletti, Enrica
CORPORATE SOURCE: Inst. Pharmacol., Univ. Milan, Milan, Italy
SOURCE: Journal of Neurochemistry (1968), 15(7), 563-75
CODEN: JONRA9; ISSN: 0022-3042
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Brain sterols from chick embryos (11 and 18 days of incubation) and mature rats, previously injected with mevalonate-2-14C, were analyzed. Acetate derivs. of the sterols were chromatographed on silica gel-Celite-AgNO3 columns. Sterol fractions were assayed for radioactivity and the amts. detd. by gas chromatog. Sterol structures were elucidated by gas chromatog.-mass spectrometry. The method used allowed the identification of some sterols representing no more than 0.01% of the total mixt. The following brain sterols were identified: cholesterol, cholestanol, cholest-5-dien-3β-ol (desmosterol); 4,4'-dimethylcholest-8-en-3β-ol, 4α-methylcholest-8-en-3β-ol, cholest-8-en-3β-ol, 4,4'-dimethylcholest-8,24-dien-3β-ol, 4α-methylcholest-8,24-dien3β-ol, cholest-8,24-dien-3β-ol and cholest-7,24-dien-3β-ol. Small amts. of other sterols including polyhydroxy sterols, were also detected. There were no qual. differences in the sterols detected in developing and mature brain. In the developing chick brain, cholesterol represented ~90% of the total sterols. In the mature rat brain, cholesterol accounted for 98% of the sterols. The adult rat brain, as well as the embryonic chick brain, demonstrated the capacity to incorporate mevalonate into cholesterol precursors and cholestanol. The sterols retaining the double in the lateral chain, that is, those of the Δ8,24 series with 29, 28, and 27 C atoms and desmosterol, were highly labeled compared with the other identified intermediates. The possibility, supported by these data, that a preferential biosynthetic route for cholesterol exists in brain, is discussed.

L4 ANSWER 40 OF 40 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text

ACCESSION NUMBER: 1963:438073 CAPLUS
DOCUMENT NUMBER: 59:38073
ORIGINAL REFERENCE NO.: 59:6869e-f
TITLE: The skin sterols of normal and triparanol-treated rats
AUTHOR(S): Clayton, R. B.; Nelson, Albert N.; Frantz, Ivan D., Jr.
CORPORATE SOURCE: Harvard Univ.
SOURCE: Journal of Lipid Research (1963), 4, 166-76
CODEN: JLPRAW; ISSN: 0022-2275
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. preceding abstr. The skin sterols of normal and triparanol (I)-treated rats were analyzed by silicic acid and gas-liquid chromatography. A no. of previously undetected compds. were found for which mol. structures were proposed on the basis of retention factors. Among these were the 4,4-dimethyl deriva. of cholest-7- and -8-enols and cholesta-8,24-dienol, and the 4α-methyl deriva. of cholesta-7,24-and 8,24-dienols. I caused accumulation of the Δ24-analogs of all the intermediates in cholesterol biosynthesis that normally occur in the 24,25-dihydro form, and increased the ratio of Δ8 as compared with Δ7 isomers.

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(FILE 'HOME' ENTERED AT 18:06:02 ON 09 FEB 2007)

FILE 'REGISTRY' ENTERED AT 18:06:11 ON 09 FEB 2007
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L2 1 S 128-33-6

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L4 40 DUP REM L3 (1 DUPLICATE REMOVED)

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18 FILES SEARCHED...
40 FILES SEARCHED...
L5 17 L4 AND (OXIDASE OR OXYGENASE OR METHYLASE OR DEMETHYL? OR METHYLTRANSFERASE OR LYASE)

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L5 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2006:951546 CAPLUS
TITLE: Metabolic flux analysis of the sterol pathway in the yeast Saccharomyces cerevisiae
AUTHOR(S): Maczek, Judith; Junne, Stefan; Nowak, Peter; Goetz, Peter
CORPORATE SOURCE: Department of Bioprocess Engineering, Institute of Biotechnology, Technical University of Berlin, Berlin, 13355, Germany
SOURCE: Bioprocess and Biosystems Engineering (2006), 29(4), 241-252
CODEN: BBEIBV; ISSN: 1615-7591
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The yeast Saccharomyces cerevisiae is a useful model system for exams. the biosynthesis of sterols in eukaryotic cells. To investigate underlying regulation mechanisms, a flux anal. of the ergosterol pathway was performed. A stoichiometric model was derived based on well known biochem. of the pathway. The model was integrated in the Software COMPFlux which uses a global optimization algorithm for the estn. of intracellular fluxes. Sterol concn. patterns were detd. by gas chromatog. in aerobic and anaerobic batch cultivations, when the sterol metab. was suppressed due to the absence of oxygen. In addn., the sterol concns.

were obsd. in a cultivation which was shifted from anaerobic to aerobic growth conditions causing the sterol pools in the cell to be filled. From time-dependent flux patterns, possible limitations in the pathway could be localized and the esterification of sterols was identified as an integral part of regulation in ergosterol biosynthesis.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2005:1300505 CAPLUS
DOCUMENT NUMBER: 144:167035
TITLE: A systematic study of yeast sterol biosynthetic protein-protein interactions using the split-ubiquitin system
AUTHOR(S): Mo, Caiqing; Bard, Martin
CORPORATE SOURCE: Department of Biology, Indiana University-Purdue University Indianapolis, Indianapolis, IN, 46202, USA
SOURCE: Biochimica et Biophysica Acta, Molecular and Cell Biology of Lipids (2005), 1737(2-3), 152-160
CODEN: BBMLPG; ISSN: 1388-1981
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sterol biosynthesis occurs in the ER and most sterol biosynthetic enzymes have transmembrane domains. However, due to difficulties in characterizing membrane protein-protein interactions, the nature of the sterol biosynthetic complex as well as in vivo interactions between various enzymes have not been described. We employed a split-ubiquitin membrane protein yeast two-hybrid system to characterize interactions between sterol biosynthetic proteins. Fourteen bait constructs were co-transformed into a reporter yeast strain with 14 prey constructs representing all sterol enzymic reactions beginning with the synthesis of squalene. Our results not only confirmed several previous interactions, but also allowed us to identify novel interactions. Based on these results, ergosterol biosynthetic enzymes display specific protein-protein interactions forming a functional complex we designate, the ergosome. In this complex, Erg11p, Erg25p, Erg27p, and Erg28p appear to form a core center that can interact with other enzymes in the pathway. Also Erg24p and Erg2p, two enzymes that are sensitive to morpholine antifungals, appear to interact with one another; however, the profile of protein interaction partners appears to be unique. Erg2p and Erg3p, two enzymes catalyzing sequential reactions also appear to have different interaction partners. Our results provide a working model as to how sterol biosynthetic enzymes are topol. organized not only in yeast but in plant and animal systems that share many of these biosynthetic reactions.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2004:1102525 CAPLUS
DOCUMENT NUMBER: 142:351946
TITLE: Disruption of ergosterol biosynthesis, growth, and the morphological transition in Candida albicans by sterol methyltransferase inhibitors containing sulfur at C-25 in the sterol side chain
AUTHOR(S): Kanagasabai, Ragu; Zhou, Wenxu; Liu, Jialin; Nguyen, Thi Thuy Minh; Veeramachaneni, Phani; Hsu, W. David
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, TX, 79409, USA
SOURCE: Lipids (2004), 39(8), 737-746
CODEN: LPDSAP; ISSN: 0024-4201
PUBLISHER: AOCS Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The sterol substrate analog 25-thialanosterol and its corresponding sulfonium salt were evaluated for their ability to serve as antifungal agents and to inhibit sterol methyltransferase (SMT) activity in Candida albicans. Both compds. inhibited cell proliferation, were fungistatic, interrupted the yeast-like-form to germ-tube-form transition, and resulted in the accumulation of zymosterol and related Δ24-sterols concurrent

with a decrease in ergosterol, as was expected for the specific inhibition of SMT activity. Feedback on sterol synthesis was evidenced by elevated levels of cellular sterols in treated vs. control cultures. However, neither farnesol nor squalene accumulated in significant amts. in treated cultures, suggesting that carbon flux is channeled from the isoprenoid pathway to the sterol pathway with minor interruption or redirection until blockage at the C-methylation step. Activity assays using solubilized C. albicans SMT confirmed the inhibitors impair SMT action. Kinetic anal. indicated that 25-thialanosterol inhibited SMT with the properties of a time-dependent mechanism-based inactivator Ki of 5 μM and apparent kinact of 0.013 min-1, whereas the corresponding sulfonium salt was a reversible-type transition state analog exhibiting a Ki of 20 nM. The results are interpreted to imply changes in ergosterol homeostasis as influenced by SMT activity can control growth and the morphol. transition in C. albicans, possibly affecting disease development.
REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2003:589448 CAPLUS
DOCUMENT NUMBER: 139:148556
TITLE: Manufacture of 7-Dehydrocholesterol and its metabolites in transgenic microorganisms expressing genes for enzymes of steroid metabolism
INVENTOR(S): Lang, Christine; Veen, Markus
PATENT ASSIGNEE(S): BASF AG, Germany
SOURCE: Ger. Offen., 120 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10203352	A1	20030731	DE 2002-10203352	20020129
WO 2003064650	A1	20030807	WO 2003-EP592	20030122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1472354	A1	20041103	EP 2003-701537	20030122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006240508	A1	20061026	US 2004-503044	20040729
PRIORITY APPLN. INFO.:			DE 2002-10203352 A	20020129
			WO 2003-EP592 W	20030122

AB 7-Dehydrocholesterol or its metabolites are manufd. in transgenic microorganisms expressing foreign genes for enzymes of steroid metab. Furthermore, the invention concerns nucleic acid constructs, as well as genetically changed organisms needed for prodn. of genetically changed organisms, in particular yeasts. A series of integrating expression constructs carrying Saccharomyces cerevisiae or mouse genes for enzymes of steroid metab., including Δ8,7 isomerase, Δ5 desaturase and Δ24 reductases were constructed and introduced into a yeast host. Several different combinations of these genes were expressed in a Saccharomyces cerevisiae. Qual. changes in patterns of steroid biosynthesis were obsd. with different combination of genes with novel steroids appearing in the hosts.

L5 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2003:589447 CAPLUS
DOCUMENT NUMBER: 139:148555
TITLE: Manufacture of zymosterol and its metabolites using

microorganisms with increased lanosterol demethylase and HMG CoA reductase activity
PATENT ASSIGNEE(S): BASF AG, Germany
SOURCE: Ger. Offen., 44 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10203346	A1	20030731	DE 2002-10203346	20020129
WO 2003064652	A1	20030807	WO 2003-EP590	20030122
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1472355	A1	20041103	EP 2003-734683	20030122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006088903	A1	20060427	US 2004-503253	20040729
PRIORITY APPLN. INFO.:			DE 2002-10203346 A	20020129
			WO 2003-EP590 W	20030122

AB A method for increasing the yield of zymosterol or its metabolites (anabolic or catabolic) in a tranegenic microorganism is described. The yield is increased by increasing the levels of lanosterol demethylase and HMG CoA reductase activity in the cell. Overexpression of a gene for a truncated HMG CoA reductase in Saccharomyces cerevisiae using the promoter of the ADH alc. dehydrogenase gene resulted in a 90-fold increase in squalene yields. Yields of several sterols were increased by 20-250%. The yield of ergosterol was not affected. Addnl. overexpression of the ERG1 lanosterol demethylase gene using the same promoter increased the yield of ergosterol and lowered yields of squalene and lanosterol.

L5 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2003:564702 CAPLUS
DOCUMENT NUMBER: 139:134671
TITLE: Enzymological properties of sterol-C4-methyl-oxidase of yeast sterol biosynthesis
AUTHOR(S): Darnet, Sylvain; Rahier, Alain
CORPORATE SOURCE: Institut de Biologie Moleculaire des Plantes, Institut de Botanique, Centre National de la Recherche Scientifique, UPR-CNRS 2357, Strasbourg, 67083, Fr.
SOURCE: Biochimica et Biophysica Acta, Molecular and Cell Biology of Lipids (2003), 1633(2), 106-117
CODEN: BBMLPG; ISSN: 1388-1981
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Despite genes of the sterol methyl-oxidase component (SMO) of the sterol-C4-demethylation multienzymic complex have been identified in a variety of organisms and the key role played by SMO in yeast sterol biosynthesis, the enzymol. properties of yeast SMO have not been investigated. An enzymic assay for measuring specifically sterol 4α-methyl-oxidase activity in Saccharomyces cerevisiae has been developed for the first time by using [14C]-4,4-dimethyl-zymosterol as substrate. It allowed enzymically formed C4-mono- and di-demethylated products to be characterized as well as two novel C4-hydroxymethyl-zymosterol derivs. to be identified as immediate oxidative metabolites by the yeast 4,4-dimethyl-zymosterol 4α-methyl-oxidase (ScSMO). The properties of microsomal ScSMO have been established with respect to cofactor requirements and kinetics and the substrate selectivity exam. with a no. of 4,4-dimethyl- and 4α-methyl-sterols. Remarkably, ScSMO showed very low activity with 24-methylene-24-dihydrocyclaartenol,

the natural substrate of maize 4,4-dimethyl-sterol-C4-methyl-oxidase. Conversely, maize sterol-C4-methyl-oxidases showed extremely reduced activity with the natural substrate of ScSMO. The previously described antifungal agent, 6-amino-2-n-pentylbenzothiazole was shown to directly inhibit the microsomal ScSMO activity in vitro. The yeast system was more than 500 times more sensitive to this deriv. than the maize systems. These distinct substrate specificities and inhibitor sensitivities between yeast and plant sterol-4α-methyl-oxidases probably reflect diversity in the structure of their active sites in relation to the distinct sterol biosynthetic pathways.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2003:147375 CAPLUS
DOCUMENT NUMBER: 139:273370
TITLE: Evidence for multiple sterol methyl transferase pathways in Pneumocystis carinii
AUTHOR(S): Zhou, Wenxu; Nguyen, Thi Thuy Minh; Collins, Margaret S.; Cushion, Melanie T.; Wea, W. David
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, TX, 79409-1061, USA
SOURCE: Lipids (2002), 37(12), 1177-1186
CODEN: LPDSAP; ISSN: 0024-4201
PUBLISHER: AOCS Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The sterol compn. of Pneumocystis carinii, an opportunistic pathogen responsible for life-threatening pneumonia in immunocompromised patients, was detd. Our purpose was to identify pathway-specific enzymes to impair using sterol biosynthesis inhibitors. Prior to this study, cholesterol (ca. 80% of total sterols), lanosterol, and several phytosterols common to plants (sitosterol and campesterol) were demonstrated in the fungus. In this investigation, we isolated all the previous sterols and many new compds. from P. carinii by culturing the microorganism in steroid-immunosuppressed rats. Thirty-one sterols were identified from the fungus (total sterol = 100 fg/cell), and seven sterols were identified from rat chow. Unusual sterols in the fungus not present in the diet included, 24(28)-methylenelanosterol, 24(28)E-ethylidene lanosterol, 24(28)Z-ethylidene lanosterol, 24β-ethyllanosta-25(27)-dienol, 24β-ethylcholest-7-enol, 24β-ethylcholesterol, 24β-ethylcholesta-5,25(27)-dienol, 24-methyllanosta-7-enol, 24-methyldesmosterol, 24(28)-methylenecholest-7-enol, 24β-methylcholest-7-enol, and 24β-methylcholesterol. The structural relationship of the 24-alkyl groups in the sterol side chain were demonstrated chromatog. relative to authentic specimens, by MS and high-resoln. 1H NMR. The hypothetical order of these compds. poses multiple phytosterol pathways that diverge from a common intermediate to generate 24β-Me or 24β-Et sterols. Formation of 24(28)E-Ethylidene lanosterol is considered to form an interrupted sterol pathway. Taken together, operation of distinct sterol methyltransferase (SMT) pathways that generate 24β-alkyl sterols in P. carinii with no counterpart in human biochem. suggests a close taxonomic affinity with fungi and provides a basis for mechanism-based inactivation of SMT enzyme to treat Pneumocystis pneumonia.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2001:126046 CAPLUS
DOCUMENT NUMBER: 134:323244
TITLE: A novel gene conserved from yeast to humans is involved in sterol biosynthesis
AUTHOR(S): Gachotte, D.; Eckstein, J.; Barbuch, R.; Hughes, T.; Roberts, C.; Bard, M.
CORPORATE SOURCE: Department of Biology, Indiana University-Purdue University Indianapolis, Indianapolis, IN, 46202, USA
SOURCE: Journal of Lipid Research (2001), 42(1), 150-154
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ERG28 gene was originally identified by microarray expression profiling as possibly involved in the Saccharomyces cerevisiae sterol pathway. Microarray analyses suggested that the transcription pattern of ERG28 closely followed that of genes involved in sterol synthesis. ERG28 was also found in Schizosaccharomyces pombe and Arabidopsis as well as humans, and in the latter was shown to be highly expressed in adult testis tissue. All four proteins contain potential transmembrane domain(s). Gas chromatog.-mass spectrometry anal. of an ERG28-deleted S. cerevisiae strain (which is slow growing but not auxotrophic for ergosterol) indicates a lesion in sterol C-4 demethylation. Sterol profiles indicate accumulation of 3-keto and carboxylic acid sterol intermediates, which are involved in removing the two C-4 Me groups from the sterol A ring. Similar intermediates have previously been demonstrated to accumulate in erg26 (sterol dehydrogenase/decarboxylase) and erg27 (3-ketoreductase) mutants in yeast. We speculate that the role of the Erg28 protein (Erg28p) may be either to tether Erg26p and Erg27p to the endoplasmic reticulum or to facilitate interaction between these proteins.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2000:628250 CAPLUS
DOCUMENT NUMBER: 133:188459
TITLE: Meiosis activating sterol augments implantation rate
INVENTOR(S): Andersen, Claus Yding; Byskov, Anne Grete
PATENT ASSIGNEE(S): Den.
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000052142	A2	20000908	WO 2000-DK80	20000225
WO 2000052142	A3	20010322		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2365225	A1	20000908	CA 2000-2365225	20000225
BR 2000008536	A	20011106	BR 2000-8536	20000225
EP 1157096	A2	20011128	EP 2000-904869	20000225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
HU 200200201	A2	20020529	HU 2002-201	20000225
JP 2002537801	T	20021112	JP 2000-602754	20000225
ZA 2001006101	A	20020204	ZA 2001-6101	20010725
US 2002042927	A1	20020411	US 2001-929800	20010814
NO 2001004120	A	20011025	NO 2001-4120	20010824
US 2005175976	A1	20050811	US 2003-626053	20030724
PRIORITY APPLN. INFO.:			DK 1999-273 A	19990226
			WO 2000-DK80 W	20000225
			US 2001-929800 B1	20010814

AB The present invention relates to the use of a new principle for improving the viability and pregnancy potential of oocytes and pre-embryos obtained in connection with in vitro fertilization and pre-embryo transfer treatment. More specifically, improvement by raising the content of Meiosis Activating Sterols (MAS) in the medium where the in vitro fertilization takes place. This is achieved by exposing and culturing one or more oocytes with spermatozoa in a culture medium comprising at least one meiosis activating sterol (MAS), a MAS analog, and/or an additive or additives capable of endogenous stimulation of the accumulation of at least one MAS. Preferred additives are FSH and EGF.

L5 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1993:97890 CAPLUS
DOCUMENT NUMBER: 118:97890
TITLE: Ergosterol depletion and 4-methyl sterols accumulation in the yeast Saccharomyces cerevisiae treated with an antifungal, 6-amino-2-n-pentylthiobenzothiazole
AUTHOR(S): Kuchta, Tomas; Bartkova, Katrina; Kubinec, Robert
CORPORATE SOURCE: Food Res. Inst., Modra, CS-90001, Czech.
SOURCE: Biochemical and Biophysical Research Communications (1992), 189(1), 85-91
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In Saccharomyces cerevisiae treated with 6-amino-2-n-pentylthiobenzothiazole, levels of ergosterol and other 4-desmethylsterols were significantly reduced. Major sterols in treated yeast were lanosterol, 4,4-dimethylzymosterol, 4-methylzymosterol, and 4-methylfecosterol. A hypothesis that the antifungal agent inhibits sterol demethylation at C-4 and forces biosynthesis to a blind pathway ending in 4-methylfecosterol is presented.

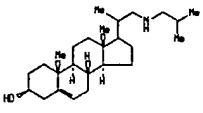
L5 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1992:526051 CAPLUS
DOCUMENT NUMBER: 117:126051
TITLE: Combined action of a fluorescent brightening agent and polyoxyethylene alkylalcohol ether on yeast
AUTHOR(S): Sugihara, Toshiharu
CORPORATE SOURCE: Fac. Educ., Gifu Univ., Gifu, 501-11, Japan
SOURCE: Nippon Kasei Gakkaishi (1992), 43(3), 207-14
CODEN: NKGAEB; ISSN: 0913-5227
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The influence of the fluorescent brightener, di-Na 4,4'-bisphenylureidostilbene-2,2'-disulfonate (I), on Saccharomyces cerevisiae yeast was investigated in the presence of a series of polyoxyethylene alkyl ethers (POEs). The nonionic surfactants changed the action of I on the yeast depending on their nature. Hydrophobic surfactants with I decreased more the growth of the yeast and the rate of surviving cells after incubation than with I alone, which was accompanied by stronger inhibition of sterol biosynthesis and of enzymes related to the electron-transport process. Extracellular enzymes were greatly enhanced in the presence of hydrophobic surfactants and I. On the other hand, the surfactants with low hydrophobicity exhibited the opposite action in reducing the influence of I on the biol. processes in yeast. POEs had little effect on yeast. The effects of POE and I on the biochem. processes of yeast correlated well with the hydrophilic-lipophilic balance (HLB) of the surfactants. This phenomenon is interpreted in terms of the change in interaction of I in POE micelles with yeast, and is supported by data on adsorption isotherms of FBA to yeast in the presence of POE.

L5 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1979:403273 CAPLUS
DOCUMENT NUMBER: 91:2273
TITLE: Azasterol inhibitors in yeast. Inhibition of the Δ24-sterol methyltransferase and the 24-methylene sterol Δ24(28)-reductase in sterol mutants of Saccharomyces cerevisiae
AUTHOR(S): Pierce, A. M.; Unrau, A. M.; Oehlschlager, A. C.; Woods, R. A.
CORPORATE SOURCE: Dep. Chem., Simon Fraser Univ., Burnaby, BC, V5A 1S6, Can.
SOURCE: Canadian Journal of Biochemistry (1979), 57(3), 201-8
CODEN: CJBIAE; ISSN: 0008-4018
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of several monoazasterols on sterol biosynthesis were examd. in the ergosterol-deficient mutants erg2, erg3, and erg5 of S. cerevisiae. When the mutants were aerobically cultured in the presence of 1 μM

23-azacholesterol, the 24-methylene sterol Δ24(28)-reductase was essentially blocked and the immediate Δ24(28)-unsatd. precursor of the final sterol metabolite in each resp. erg strain was found to accumulate. Total sterol prodn. was enhanced in the cultures grown in the presence of 1 μM 23-azacholesterol. In cultures which were grown in the presence of 1 μM 25-azacholesterol, which effectively blocked the Δ24-sterol methyltransferase, all 3 erg strains accumulated zymosterol as the major sterol component with lesser quantities of predicted terminal sterols. Mutant erg2 (block at Δ8→Δ7 isomerase) grew poorly in the presence of 1 μM 25-azacholesterol and produced low levels of cholesta-5,8,24-trienol and cholesta-5,8,22,24-tetraenol, which were isolated and characterized. Compared with controls, erg2 treated with 1 μM 23-azacholesterol produced increased amts. of ergosta-5,8,22,24(28)-tetraenol, which was hitherto unidentified as a yeast sterol. In erg5 (block at Δ22-dehydrogenase) treatment with 1 μM 25-azacholestanol effectively blocked the Δ24-sterol methyltransferase and resulted in increased total sterol prodn. Cholesta-5,7,24-trienol accounted for 27-9% of the sterol pool in 25-azasterol inhibited erg5 cultures. The 25-azasterol-inhibited erg5 mutant thus provides a source of cholesta-5,7,24-trienol, a potential provitamin D3 substitute.

L5 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1979:50484 CAPLUS
DOCUMENT NUMBER: 90:50484
TITLE: Involvement of cytochrome P-450 and a cyanide-sensitive enzyme in different steps of lanosterol demethylation by yeast microsomes
AUTHOR(S): Ohba, Masayuki; Sato, Ryo; Yoshida, Yuzo; Nishino, Tokuzo; Katsuki, Hirohiko
CORPORATE SOURCE: Inst. Protein Res., Osaka Univ., Suita, Japan
SOURCE: Biochemical and Biophysical Research Communications (1978), 85(1), 21-7
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the presence of NADPH, NAD, and O2, microsomes prepd. from Saccharomyces cerevisiae converted lanosterol-1,7,15,22, 26,30-14C to 4,4-dimethylzymosterol, 4-methylzymosterol, and zymosterol. This conversion was accompanied by the liberation of 14CO2 derived from the Me group (C-30) at the 4-position. 14CO2 formation was inhibited by antibodies to yeast cytochrome P 450 and by CN-. Gas chromatog. indicated that the antibodies inhibited the conversion of lanosterol to 4,4-dimethylzymosterol, whereas the demethylation of the latter to 4-methylzymosterol was sensitive to CN-. Thus, cytochrome P 450 and a CN--sensitive enzyme are involved in the CN--sensitive enzyme are involved in the 14α- and 4-demethylations of lanosterol, resp., by yeast microsomes.

L5 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1978:500829 CAPLUS
DOCUMENT NUMBER: 89:100829
TITLE: Azasterol inhibitors in yeast. Inhibition of the 24-methylene sterol Δ24(28)-reductase and Δ24-sterol methyltransferase of Saccharomyces cerevisiae by 23-azacholesterol
AUTHOR(S): Pierce, H. D., Jr.; Pierce, A. M.; Srinivasan, R.; Unrau, A. M.; Oehlschlager, A. C.
CORPORATE SOURCE: Dep. Chem., Simon Fraser Univ., Burnaby, BC, Can.
SOURCE: Biochimica et Biophysica Acta, Lipids and Lipid Metabolism (1978), 529(3), 429-37
CODEN: BBLLA6; ISSN: 0005-2760
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The effects of 23-azacholesterol (I) [29588-39-4] on sterol biosynthesis and growth of S. cervisiae were exam. In the presence of 0.2, 0.5, and 1 μM I, aerobically-growing yeast produced a nearly const. amt. of ergosta-5,7,22,24(28)-tetraen-33-ol [7720-30-1] (~36% of total sterol) and slowly accumulated zymosterol [128-33-6] with a concomitant decline in ergosterol [57-87-4] synthesis. Growth and total sterol content of yeast cultures treated with 0.2-1 μM I were similar to that of the control culture. Yeast cultures treated with 5 and 10 μM I produced mostly zymosterol (58-61% of total sterol), whereas ergosta-5,7,22,24(28)-tetraenol prodn. declined to <10% of total sterol. The obsd. changes in the distribution of sterols in treated cultures are consistent with inhibition of 24-methylene sterol 24(28)-reductase [56445-82-4] (total inhibition at 1 μM I) and of Δ24-sterol methyltransferase [37257-07-1] (71% inhibition at 10 μM I). Yeast cultures treated with 10 μM I contained 4,4-dimethyl-5α-cholesta-8,14,24-trien-3β-ol [64284-64-6] and 4α-methyl-5α-cholesta-8,14,24-trien-3β-ol [67445-13-0], which were isolated and characterized for the first time.

L5 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1978:419944 CAPLUS
DOCUMENT NUMBER: 89:19944
TITLE: Sterol biosynthesis by strains of Saccharomyces cerevisiae in the presence and absence of dissolved oxygen
AUTHOR(S): Aries, Vivienne; Kirsop, B. H.
CORPORATE SOURCE: Brew. Res. Found., Nutfield/Redhill/Surrey, UK
SOURCE: Journal of the Institute of Brewing (1978), 84(2), 118-22
CODEN: JINBAL; ISSN: 0368-2587
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The content of sterols in S. cerevisiae which has been harvested after anaerobic growth and then added to a complex nutrient medium, rises rapidly from ca. 1 mg/g dry yeast to ca. 10 mg in the presence of dissolved O. A range of sterols, present principally as sterol esters, is formed during this period. The concn. of free sterols does not rise above 3 mg/g and esters are thought to form a reserve sterol pool. Cyclization of squalene to lanosterol [79-63-0] in the presence of O seems not to be markedly affected by O concn. in contrast to demethylation and desatn. reactions on the pathway to ergosterol [57-87-4]. When O concn. falls to zero, further metab. of preformed sterols continues, with the accumulation of episterol [474-68-0] and ergosterol and redn. in the concn. of zymosterol [128-33-6] and 24(28)-dehydroergosterol [7720-30-1]. During anaerobic growth a marked hydrolysis of sterol esters occurs and free sterols eventually predominate.

L5 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1975:590211 CAPLUS
DOCUMENT NUMBER: 83:190211
TITLE: Nuclear demethylation and C-24 alkylation during ergosterol biosynthesis in Saccharomyces cerevisiae
AUTHOR(S): Fryberg, M.; Avruch, L.; Oehlschlager, A. C.; Unrau, A. M.
CORPORATE SOURCE: Dep. Chem., Simon Fraser Univ., Burnaby, BC, Can.
SOURCE: Canadian Journal of Biochemistry (1975), 53(8), 861-9
CODEN: CJBIAE; ISSN: 0008-4018
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The role of 4,4-dimethylzymosterol (I), 4,4-dimethylfecosterol (II) and 31-norlanosterol (III) in the biosynthesis of ergosterol (IV) in S. cerevisiae has been investigated. The synthesis of II and III coupled with the availability of I facilitated a search for these sterols in com. yeast sterol concs., fresh lab. grown yeast and fresh brewery grown yeast. II was not detected in any of these mixts. whereas III was found in the 1st and last and I was present in all 3 sources investigated. Investigation of incorporation of lanosterol-2-3H into I, II, and III revealed significant incorporation into I but neither II nor III. This observation suggests the principle pathway for ergosterol biosynthesis initially involved lanosterol → I → 4α-methylzymosterol (V). Incubation of a mixt. of zymosterol-2,4-3H and lanosterol-26,27-14C with S. cerevisiae revealed that during the initial phases of aerobic growth the major route from V to IV involves zymosterol VI but as VI accumulates 4α-methyl-24-methylenezymosterol assumes equal importance.

L5 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1970:506548 CAPLUS
DOCUMENT NUMBER: 73:106548
TITLE: S-adenosylmethionine: Δ24-sterol methyltransferase in ergosterol biosynthesis in yeast. Specificity of sterol substrates and inhibitors
AUTHOR(S): Moore, J. Thomas, Jr.; Gaylor, James L.
CORPORATE SOURCE: Grad. Sch. of Nutr., Cornell Univ., Ithaca, NY, USA
SOURCE: Journal of Biological Chemistry (1970), 245(18), 4684-8
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The role of an S-adenosylmethionine:Δ24-sterol methyltransferase (methyltransferase) in ergosterol biosynthesis in yeast has been investigated. Sterol substrate specificity studies indicate that zymosterol is the best Me group acceptor in the methyltransferase assay. 4-Me sterols are very poor substrates; sterols with a fully reduced side chain (i.e. no double bond at C-26) are not methylated. A corresponding 3-ketosteroid, 5α-cholesta-8,24-dien-3-one, was methylated at a slower rate; similarly, sterols with nuclear double bonds in positions 5 or 5 and 7 were poorer substrates than zymosterol. Inhibition studies indicate that sterols with a satd. isooctyl side chain are competitive inhibitors of zymosterol in the methyltransferase reaction. Sterols that possess an alkylated side chain markedly altered the rate of methyltransfer; at low concns. of substrate, addn. of 24-alkyl-substituted sterols stimulated the methyltransferase, whereas at higher concns. of substrate the 24-alkyl sterols were inhibitory.

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FILE 'REGISTRY' ENTERED AT 18:06:11 ON 09 FEB 2007
L1 1 S 7448-02-4
L2 1 S 128-33-6

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L4 40 DUP REM L3 (1 DUPLICATE REMOVED)
L5 17 S L4 AND (OXIDASE OR OXYGENASE OR METHYLASE OR DEMETHYL? OR ME

=> s (11 OR 12) AND (oxidase OR oxygenase OR methylase OR demethyl? OR methyltransferase OR 1
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L7 109 L6 NOT L3

=> s 17 AND (demethylat? OR methylat?)
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35 FILES SEARCHED...
L8 47 L7 AND (DEMETHYLAT? OR METHYLAT?)

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L8 ANSWER 1 OF 47 AGRICOLA Compiled and distributed by the National
Full Text
Agricultural Library of the Department of Agriculture of the United States of America. It contains copyrighted materials. All rights reserved. (2007) on STN
ACCESSION NUMBER: 1998:2009 AGRICOLA
DOCUMENT NUMBER: IND20608185
TITLE: Identification of cDNAs encoding sterol methyl-transferases involved in the second methylation step of plant sterol biosynthesis.
AUTHOR(S): Bouvier-Nave, P.; Husselstein, T.; Desprez, T.; Benveniste, P.
CORPORATE SOURCE: Institut de Botanique, Strasbourg, France.
AVAILABILITY: DNAL (QP501.E8)
SOURCE: European journal of biochemistry, June 1997. Vol. 246, No. 2. p. 518-529
Publisher: Berlin : Springer-Verlag Berlin.
CODEN: EJBCAI; ISSN: 0014-2956
NOTE: Includes references
PUB. COUNTRY: Germany
DOCUMENT TYPE: Article
FILE SEGMENT: Non-U.S. Imprint other than FAO
LANGUAGE: English
AB Two methyl transfers are involved in the course of plant sterol biosynthesis and responsible for the formation of 24-alkyl sterols (mainly 24-ethyl sterols) which play major roles in plant growth and development. The first methyl transfer applies to cycloartenol, the second one to 24-methylene lophenol. Five cDNA clones encoding two Arabidopsis thaliana, two Nicotiana tabacum and one Ricinus communis S-adenosyl-L-methionine (AdoMet) sterol methyltransferases (SMT) were isolated. The deduced amino acid sequences of A. thaliana and N. tabacum SMT are about 80% identical in all possible combinations. In contrast they are about 40% identical with the deduced amino acid sequence of R. communis SMT and the published Glycine max sequence. Both A. thaliana and one N. tabacum SMT cDNAs were expressed in a yeast null mutant erg6, deficient in AdoMet zymosterol C24-methyltransferase and containing C24-non-alkylated sterols. In all cases, several 24-ethylidene sterols were synthesized. A thorough study of the sterolic composition of erg6 expressing the A. thaliana cDNA 411 (erg6-411B-pYeDP60) showed 24-methylene and 24-ethylidene derivatives of 4-desmethyl, 4alpha-methyl and 4,4-dimethyl sterols as well as 24-methyl and 24-ethyl derivatives of 4-desmethyl sterols. The structure of 5alpha-stigmasta-8, Z-24(24')-dien-3beta-ol, the major sterol of transformed yeasts, was demonstrated by 400 MHz 1H NMR. Microsomes from erg6-411B-pYeDP60 were shown to possess AdoMet-dependent sterol-C-methyltransferase activity. Delipidated preparations of these microsomes converted cycloartenol into 24-methylene cycloartanol and 24-methylene lophenol into 24-ethylidene lophenol, thus allowing the first identification of a plant sterol-C-methyltransferase cDNA. The catalytic efficiency of the expressed SMT was 17-times higher with 24-methylene lophenol than with cycloartenol. This result provides evidence that the A. thaliana cDNA 411 (and most probably the 3 plant SMT cDNAs presenting 80% identity with it) encodes a 24-methylene lophenol-C-24 1 methyltransferase catalyzing the second methylation step of plant sterol biosynthesis.

L8 ANSWER 2 OF 47 AGRICOLA Compiled and distributed by the National
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Agricultural Library of the Department of Agriculture of the United States of America. It contains copyrighted materials. All rights reserved. (2007) on STN
ACCESSION NUMBER: 96:15445 AGRICOLA
DOCUMENT NUMBER: IND20500737
TITLE: Cloning and characterization of ERG25, the

Saccharomyces cerevisiae gene encoding C-4 sterol methyl oxidase.
AUTHOR(S): Bard, M.; Bruner, D.A.; Pierson, C.A.; Lees, N.D.; Biermann, B.; Frye, L.; Koegel, C.; Barbuch, R.
CORPORATE SOURCE: Indiana University-Purdue University at Indianapolis, Indianapolis, IN.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, Jan 9, 1996. Vol. 93, No. 1. p. 186-190
Publisher: Washington, D.C. : National Academy of Sciences,
CODEN: PNASA6; ISSN: 0027-8424
NOTE: Includes references
PUB. COUNTRY: District of Columbia; United States
DOCUMENT TYPE: Article; Conference
FILE SEGMENT: U.S. Imprints not USDA, Experiment or Extension
LANGUAGE: English
AB We have cloned the Saccharomyces cerevisiae C-4 sterol methyl oxidase ERG25 gene. The sterol methyl oxidase performs the first of three enzymic steps required to remove the two C-4 methyl groups leading to cholesterol (animal), ergosterol (fungal), and stigmasterol (plant) biosynthesis. An ergosterol auxotroph, erg25, which fails to demethylate and concomitantly accumulates 4,4-dimethylzymosterol, was isolated after mutagenesis. A complementing clone consisting of a 1.35-kb Dra I fragment encoded a 309-amino acid polypeptide (calculated molecular mass, 36.48 kDa). The amino acid sequence shows a C-terminal endoplasmic reticulum retrieval signal KKXX and three histidine-rich clusters found in eukaryotic membrane desaturases and in a bacterial alkane hydroxylase and xylene monooxygenase. The sterol profile of an ERG25 disruptant was consistent with the erg25 allele obtained by mutagenesis.

L8 ANSWER 3 OF 47 AGRICOLA Compiled and distributed by the National
Full Text
Agricultural Library of the Department of Agriculture of the United States of America. It contains copyrighted materials. All rights reserved. (2007) on STN
ACCESSION NUMBER: 93:21059 AGRICOLA
DOCUMENT NUMBER: IND93008682
TITLE: Ergosterol depletion and 4-methyl sterols accumulation in the yeast Saccharomyces cerevisiae treated with an antifungal 6-amino-2-n-pentylthiobenzothiazole.
AUTHOR(S): Kuchta, T.; Bartkova, K.; Kubinec, R.
CORPORATE SOURCE: Food Research Institute, Modra, Czechoslovakia
AVAILABILITY: DNAL (442.8 B5236)
SOURCE: Biochemical and biophysical research communications, Nov 30, 1992. Vol. 189, No. 1. p. 85-91
Publisher: Orlando, Fla. : Academic Press.
ISSN: 0006-291X
NOTE: Includes references.
DOCUMENT TYPE: Article
FILE SEGMENT: U.S. Imprints not USDA, Experiment or Extension
LANGUAGE: English
AB In Saccharomyces cerevisiae treated with an antifungal agent, 6-amino-2-n-pentylthiobenzothiazole, levels of ergosterol and other 4-desmethylsterols were found to be significantly reduced. Major sterols in treated yeast were lanosterol, 4,4-dimethylzymosterol, 4-methylzymosterol and 4-methylfecosterol. A hypothesis is stated that the antifungal agent inhibits sterol demethylation at C-4 and forces the biosynthesis to a blind pathway ending by 4-methylfecosterol.

L8 ANSWER 4 OF 47 AGRICOLA Compiled and distributed by the National
Full Text
Agricultural Library of the Department of Agriculture of the United States of America. It contains copyrighted materials. All rights reserved. (2007) on STN
ACCESSION NUMBER: 81:34471 AGRICOLA
DOCUMENT NUMBER: IND81028623
TITLE: Involvement of cytochrome b5 and a cyanide-sensitive monooxygenase in the 4-demethylation of 4,4-dimethylzymosterol by yeast microsomes Saccharomyces cerevisiae.
AUTHOR(S): Aoyama, Y.; Yoshida, Y.; Sato, R.; Susani, M.; Ruis, H.
AVAILABILITY: DNAL (381 B522)
SOURCE: Biochimica et biophysica acta., Jan 26, 1981 Vol. 663, No. 1. p. 194-202 ill
Publisher: Amsterdam, Elsevier/North-Holland.
ISSN: 0006-3002
NOTE: 26 ref.
DOCUMENT TYPE: Article
FILE SEGMENT: Non-U.S. Imprint other than FAO
LANGUAGE: English

L8 ANSWER 5 OF 47 BIOTECHNO COPYRIGHT 2007 Elsevier Science B.V.
Full Text
on STN
ACCESSION NUMBER: 2003:37393370 BIOTECHNO
TITLE: Sterol methyltransferase2: Purification, properties, and inhibition
AUTHOR: Zhou W.; Nes W.D.
CORPORATE SOURCE: W.D. Nes, Dept. of Chemistry and Biochemistry, Texas Tech. University, Lubbock, TX 79409-1061, United States.
E-mail: wdavid.nes@ttu.edu
SOURCE: Archives of Biochemistry and Biophysics, (01 DEC 2003), 420/1 (18-34), 42 reference(s)
CODEN: ABBIA4 ISSN: 0003-9861
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:37393370 BIOTECHNO
AB Expression of the Arabidopsis sterol methyltransferase2 (SMT2) cDNA in Escherichia coli yields a native protein, when purified to homogeneity, has the predicted molecular mass ca. 40kDa on SDS-PAGE and recognizes native sterols synthesized by Arabidopsis with a Δ^{24}(25)-bond (cycloartenol; K_m 35μM and k_{cat} 0.001s^{-1}) and Δ^{24}(25)-bond^{sat}24(28)-methylenelophenol; K_m 28μM and k_{cat} 0.01s^{-1}). Cycloartenol was converted to a single olefinic product-24(28)-methylenecycloartanol whereas 24(28)-methylenelophenol was converted to a mixture of three stereochemically related products with the Δ^{24}(28)Z-ethylidene, Δ^{24}(28)E-ethylidene, and Δ^{25}(27)-24β-ethyl side chains. Structural determinants essential to activity were the nucleophilic features at C-3 and C-24. The double bond position in the sterol substrate influenced catalytic efficiency according to the order: side chain, Δ^{24}(25)<Δ^{24}(28)<nucleus, Δ^{7}<Δ^{5}=9,19-cyclopropane. The 14α-methyl group was harmful to catalysis, reducing the suitability of cycloartenol as a substrate. On the basis of substrate activity and product distribution, SMT action was probed further using substrate (26,27-dehydrozymosterol: 26,27-DHZ) and intermediate (25-azacycloartenol: 25-AC) analogs of the SMT-catalyzed reactions. 26,27-DHZ was C-methylated to 26-homocholesta-8(9), 23(24)E, 26(26')-trienol as well as 26-homocholesta-8(9),26(26')-3β, 24β-dienol by SMT2, K_m of 15μM, k_{cat} of 0.001s^{-1}. In addition, 26,27-DHZ acted as a mechanism-based irreversible inhibitor that results in the specific covalent modification of SMT2, exhibiting K_i of 49μM, k_{inact} of 0.009s^{-1} and partition ratio of 0.11. Substrate protection with zymosterol, 24(28)-methylenelophenol against 26,27-DHZ and similar inhibition of the first and second $C_{1-transfer}$ activities by the reversible inhibitor 25-AC of K_i 20nM suggested the analogs interacted at the same active site. [28E-^{2H}]- and [28Z-^{2H}]24(28)-methylenelanosterols were paired with AdoMet and differences of $^{2H-incorporation}$ in the enzyme-generated 24-ethyl olefins supported an antimechanism. The results suggest plant SMT2 has a position-specific substrate specificity for $\Delta^{24(25)}$-sterols and contains a single active center to catalyze the consecutive $C_{1-transfer}$ activities by substrate reaction channels similar to the fungal SMT1. © 2003 Elsevier Inc. All rights reserved.

L8 ANSWER 6 OF 47 BIOTECHNO COPYRIGHT 2007 Elsevier Science B.V.
Full Text
on STN
ACCESSION NUMBER: 2003:36851636 BIOTECHNO
TITLE: Enzymological properties of sterol-C4-methyl-oxidase of yeast sterol biosynthesis
AUTHOR: Darnet S.; Rahier A.
CORPORATE SOURCE: A. Rahier, Ctr. Natl. de la Rech. Scientifique, Institut de Botanique, UPR-CNRS 2357, 28 rue Goethe, 67083 Strasbourg Cedex, France.
E-mail: enzymo@cbta-ulp.u-strasbg.fr
SOURCE: Biochimica et Biophysica Acta - Molecular and Cell Biology of Lipids, (21 JUL 2003), 1633/2 (106-117), 34 reference(s)
CODEN: BBMLFG ISSN: 1388-1981
DOCUMENT TYPE: Journal; Article
COUNTRY: Netherlands
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:36851636 BIOTECHNO
AB Despite genes of the sterol methyl-oxidase component (SMO) of the sterol-C4-demethylation multienzymatic complex have been identified in a variety of organisms and the key role played by SMO in yeast sterol biosynthesis, the enzymological properties of yeast SMO have not been investigated. An enzymatic assay for measuring specifically sterol 4α-methyl-oxidase activity in Saccharomyces cerevisiae has been developed for the first time by using [^{14}C]-4,4-dimethyl-zymosterol as substrate. It allowed enzymatically formed C4 mono- and di-demethylated products to be characterized as well as two novel C4-hydroxymethyl-zymosterol derivatives to be identified as immediate oxidative metabolites by the yeast 4,4-dimethyl-zymosterol 4α-methyl-oxidase (ScSMO). The properties of microsomal ScSMO have been established with respect to cofactor requirements and kinetics and the substrate selectivity examined with a number of 4,4-dimethyl- and 4α-methyl-sterols. Remarkably, ScSMO showed very low activity with 24-methylene-24-dihydrocycloartenol, the natural substrate of maize 4,4-dimethyl-sterol-C4-methyl-oxidase. Conversely, maize sterol-C4-methyl-oxidases showed extremely reduced activity with the natural substrate of ScSMO. The previously described antifungal agent, 6-amino-2-n-pentylbenzothiazole was shown to directly inhibit the microsomal ScSMO activity in vitro. The yeast system was more than 500 times more sensitive to this derivative than the maize systems. These distinct substrate specificities and inhibitor sensitivities between yeast and plant sterol-4α-methyl-oxidases probably reflect diversity in the structure of their active sites in relation to the distinct sterol biosynthetic pathways. © 2003 Elsevier B.V. All rights reserved.

L8 ANSWER 7 OF 47 BIOTECHNO COPYRIGHT 2007 Elsevier Science B.V.
Full Text
on STN
ACCESSION NUMBER: 1999:29124671 BIOTECHNO
TITLE: Site-directed mutagenesis of the sterol methyl transferase active site from Saccharomyces cerevisiae results in formation of novel 24-ethyl sterols
AUTHOR: Nes W.D.; McCourt B.S.; Marshall J.A.; Ma J.; Dennis A.L.; Lopez M.; Li H.; He L.
CORPORATE SOURCE: W.D. Nes, Department of Chemistry/Biochemistry, Texas Tech University, Lubbock, TX 79409, United States.
E-mail: wDnes@ttacs.ttu.edu
SOURCE: Journal of Organic Chemistry, (05 MAR 1999), 64/5 (1535-1542)
CODEN: JOCEAH ISSN: 0022-3263
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1999:29124671 BIOTECHNO
AB Δ(24(28))-Sterols are end products of a mono C-methylation pathway catalyzed by the native Δ(24(25))- to Δ(24(28))-sterol methyl transferase (SMT) enzyme from Saccharomyces cerevisiae. Using a Tyr^{81} to Phe mutant SMT enzyme of S. cerevisiae, generated by site-directed mutagenesis of a highly conserved residue in the sterol binding site, we found that several Δ(24(25))- and Δ(24(28))-sterols, which are not substrates for the native protein, were catalyzed to mono- and bis-C24-alkylated side chains. The mutant protein behaved similarly to the native protein in chromatography and in binding zymosterol, the preferred substrate. Zymosterol was converted to fecosterol by the Y81F mutant protein with similar turnover efficiency as the native protein (K(m) = 12 μM and k(cat) = 0.01 s^{-1}); trace 24-ethyl sterols were detected from these incubations. 4α-Methyl zymosterol, which is not a normal substrate for the wild-type SMT enzyme, was converted to 4α- methy fecosterol in high yield. When fecosterol and 4α-methyl fecosterol were assayed individually at saturating concentrations only fecosterol served as an effective substrate for the second C-transfer step (K(m) = 38 μM and k(cat) = 0.002 s^{-1}), suggesting that successive C-methylation of Δ(24(28))-substrates is limited by product release and that molecular recognition of sterol features involves hydrogen bond formation. Isomeric 24- ethyl sterol olefins generated from 24(28)-methylene cholesterol were characterized by chromatographic (GC and HPLC) and spectral methods (MS and ^{1H} NMR), viz., fucosterol, isofucosterol, and clerosterol. Changes in rate of C-methylation and product distributions resulting from deuterium substitution at C28 were used to establish the kinetic isotope effects (KIEs) for the various deprotonations leading to C24-methylene, C24-ethylidene, and C24-ethyl sterols. An isotope effect on C28 methyl deprotonation generated during the first $C_{1-transfer}$ was detected with zymosterol and desmosterol paired with AdoMet^{2H} and ^{2H}AdoMet. A similar $^{2H-incorporation}$ experiment to test for a KIE generated during the second $C_{1-transfer}$ reaction with AdoMet paired with 24(28)-methylenecholesterol and c28-^{2H};24(28)-methylene cholesterol indicated an inverse isotope effect associated with C27 deprotonation. Alteration in the proportion of the C24 alkylated olefinic products generated by the pure Y81F mutant resulted from the suppression of the formation of Δ(24(28))-ethyl sterols (C28 deprotonation) by a primary deuterium isotope effect with a compensating stimulation of the formation of 24-ethyl sterols (C27 deprotonation). Kinetic study on the rate of product formation indicated a normal KIE of k(H)/k(D) = 2.62 for the first $C_{1-transfer}$. Alternatively, an inverse KIE was established with k(H)/k(D) = 0.91 for the second $C_{1-transfer}$ resulting from conversion of the 24(28)-double bond (sp^2 hybridization) to a 24β-ethyl group (sp^3 hybridization). From the structures and stereochemical assignments of the C-ethyl olefin products, the stereochemistry of the attack of AdoMet in the second $C_{1-transfer}$ was found to operate a Si-face (backside) attack at C24, analogous to the first C_1 transfer reaction.

L8 ANSWER 8 OF 47 BIOTECHNO COPYRIGHT 2007 Elsevier Science B.V.
Full Text
on STN
ACCESSION NUMBER: 1997:27417244 BIOTECHNO
TITLE: Cholesterol biosynthesis from lanosterol: Development of a novel assay method and characterization of rat liver microsomal lanosterol Δ^{24}-reductase
AUTHOR: Bae S.-H.; Paik Y.-K.
CORPORATE SOURCE: Y.-K. Paik, Department of Biochemistry, College of Science, Yonsei University, Seoul 120-749, South Korea.
SOURCE: Biochemical Journal, (1997), 326/2 (609-616), 31 reference(s)
CODEN: BIJOAK ISSN: 0264-6021
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1997:27417244 BIOTECHNO
AB The membrane-bound sterol $\Delta^{24-reductase}$ (24-reductase) catalyses anaerobic reduction of the 24(25)-enes of lanosterol and other obligatory intermediates of cholesterol biosynthesis from lanosterol. A novel assay method and properties of the 24-reductase are described. More than a 120-fold induction of the 24-reductase activity was achieved by

feeding rats a diet containing 5% cholestyramine plus 0.1% lovastatin in chow and by modulating diurnal variation. With this enzyme induction condition, lanosterol was converted efficiently into dihydrolanosterol in both intact hepatic microsomes and freshly isolated hepatocytes only when either miconazole or CO was added to inhibit 14α-demethylation of lanosterol. AR45 cells, which are deficient in 14α-methyl demethylase (14α-DM), exhibit lanosterol 24-reductase activity without addition of either CO or miconazole. Conversely, inhibition of the 24-reductase was not required for the expression of 14α-DM activity. Studies on the substrate specificities for the 24-reductase using different 24(25)-enes showed that the most reactive substrate was 5α-cholesta-7,24-dien-3β-ol, which exhibited a maximal 18-fold higher k(cat) than that of lanosterol without the aid of the 14α-DM inhibitor. In addition, both the kinetic behaviour of lanosterol substrate in relation to the 24-reductase and a non-competitive inhibition mode of U18666A (K(i) 0.157 μM) as well as Triparanol (K(i) 0.523 μM), two well-known 24-reductase inhibitors, were determined. On the basis of our new findings on the preferred substrate and on the negative effect of 14α-DM on the 24-reductase, we suggest that C-24 reduction of sterols takes place straight after sterol Δ(8 → 7) isomerization of zymosterol, which occurs several steps after C-32 demethylation of lanosterol in the 19-step pathway of cholesterol biosynthesis from lanosterol.

L8 ANSWER 9 OF 47 BIOTECHNO COPYRIGHT 2007 Elsevier Science B.V.
Full Text
on STN
ACCESSION NUMBER: 1997:27246661 BIOTECHNO
TITLE: Stereochemistry of Yeast $\Delta^{24\text{-sterol}}$ methyl transferase
AUTHOR: Acuna-Johnson A.P.; Oehlschlager A.C.; Pierce A.M.; Pierce H.D. Jr.; Czyzewska E.K.
CORPORATE SOURCE: A.C. Oehlschlager, Department of Chemistry, Simon Fraser University, Burnaby, BC V5A 1S6, Canada.
SOURCE: Bioorganic and Medicinal Chemistry, (1997), 5/5 (821-832), 44 reference(s)
CODEN: BMECEP ISSN: 0968-0896
PUBLISHER ITEM IDENT.: S0968089697000102
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1997:27246661 BIOTECHNO
AB S-Adenosyl-l-methionine:Δ24-sterol methyl transferase (24-SMT) mediates introduction of the C-28 carbon of yeast sterols. It has been shown that sulfonium analogues of the presumptive cationic intermediates of the methylenation reaction are potent in vivo and in vitro inhibitors of this process. In the presence of these inhibitors, cultures of yeast produced increased proportions of zymosterol, the natural substrate of the enzyme, while proportions of ergosterol and ergostatetraenol were decreased. New C27-sterol metabolites were also found. The in vivo inhibitory power of the analogues (I_{50} (μM)! was determined from the proportion of C-24 methylated sterols to C-24 nonmethylated sterols in treated cultures to be in the following order: 25-thiacholesteryl iodide (0.07) > 24(S)-methyl-25-thiacholesteryl iodide (0.14) > 24(R)-methyl-25-thiacholesteryl iodide (0.25). kinetic inhibition as revealed by radiolabeled S-adenosyl-l-methionine (SAM), crude enzyme and 25-thiacholesteryl iodide revealed this inhibitor to be uncompetitive with respect to zymosterol and competitive with respect to SAM. The greater inhibitory power of 24(S)-methyl-25-thiacholesteryl iodide compared to 24(R)-methyl-25-thiacholesteryl iodide suggests that methyl donation to Δ^{24} occurs from the si face. When considered in conjunction with Arigoni's previous work, the present results infer the methylenation mediated by yeast 24-SMT proceeds by alkylation from the si face of Δ^{24} followed by migration of a hydrogen from C-24 to C-25 across the re face and final loss of a hydrogen from C-28 on the re face.

L8 ANSWER 10 OF 47 BIOTECHNO COPYRIGHT 2007 Elsevier Science B.V.
Full Text
on STN
ACCESSION NUMBER: 1985:15040692 BIOTECHNO

TITLE: Sterols of ketoconazole-inhibited Leishmania mexicana mexicana promastigotes
AUTHOR: Goad L.J.; Holz Jr. G.G.; Beach D.H.
CORPORATE SOURCE: Department of Biochemistry, University of Liverpool, Liverpool L69 3BX, United Kingdom.
SOURCE: Molecular and Biochemical Parasitology, (1985), 15/3 (257-279)
CODEN: MBIPDP
DOCUMENT TYPE: Journal; Article
COUNTRY: Netherlands
LANGUAGE: English
AN 1985:15040692 BIOTECHNO
AB Leishmania mexicana mexicana promastigotes grown with cholesterol, supplied in natural products as the free sterol and as cholesteryl esters, were exposed to e2-^{14C}]mevalonate and to the antimycotic drug ketoconazole. Growth was inhibited and cholesterol and 14α-methyl sterols accumulated in free and esterified forms (cholesterol >>>4α,14α-dimethylcholesta-8,24-dien-3β-ol>>14α-methylcholesta-8,24- dien-3β-ol .simeq. 14α-methylergosta-8,24(28)-dien-3β-ol >>4α,14α-dimethylergosta-8,24(28)-dien-3β-ol; identified by capillary gas chromatography/mass spectrometry, and by ^{1H} and ^{13C} nuclear magnetic resonance spectrometry). The 14α-methyl sterols were preferentially labelled with ^{14C}. The cholesterol was unlabelled and substituted for a substantial fraction of the major product of sterol biosynthesis, ergosta-5,7,24(28)-trien-3β-ol (5-dehydroepisterol), but did not replace it and did not offer remarkable protection against either growth inhibition or alteration of sterol biosynthesis. Promastigotes grown with c6-^{3H}]cholesterol or c4-^{14C}]cholesterol did not contain labelled forms of Leishmania sterols, or other sterols. The chromatographic and spectrometric sterol analyses and the isotopic tracer findings suggested that ketoconazole impaired the cytochrome P-450 dependent 14α-demethylation of lanosterol, that cholesterol was neither biosynthesized nor metabolized, and that the physiological functions of 5-dehydroepisterol had sterol structural requirements not entirely met by cholesterol. In all these studies, L. mexicana mexicana demonstrated a sterol biochemistry remarkably similar to that of fungi. This recommends an increase in interest in antimycotic drugs as chemotherapeutic agents for leishmanial infections.

L8 ANSWER 11 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2005:1149200 CAPLUS
DOCUMENT NUMBER: 144:461112
TITLE: Enzyme redesign and interactions of substrate analogues with sterol methyltransferase to understand phytosterol diversity, reaction mechanism and the nature of the active site
AUTHOR(S): Nes, W. D.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, TX, 79409-1061, USA
SOURCE: Biochemical Society Transactions (2005), 33(5), 1189-1196
CODEN: BCSTB5; ISSN: 0300-5127
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several STM (sterol methyltransferase) genes have been cloned, sequenced and expressed in bacteria recently, making it possible to address questions of the relationship between sterol structure and function. The active site and mechanism of action of a set of phylogenetically diverse SMTs have been probed by site-directed mutagenesis as well as by using substrate and related analogs of the SMT-catalyzed reaction. An active-site model has been developed that is in accord with the results presented, which is consistent with the hypothesis that SMTs are bifunctional enzymes kinetically responsible to bind Δ24-acceptor sterols of specific steric and electronic character and rigid orientation imposed by multiple hydrophobic active site contacts exacted from a common waxy core. Functional divergence influenced by the architectural role of sterols in membranes is considered to govern the evolution of product distribution and specificity of individual SMTs as discussed.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2005:824127 CAPLUS
DOCUMENT NUMBER: 144:370270
TITLE: Electronic and structural features of lanosterol in the 14α-demethylation
AUTHOR(S): Cabrera-Vivas, B. M.; Pineda, Flor P.; Garcia-Hidalgo, Sandra; Melendez, F. J.; Reyes-Ortega, Y.; Ramirez, Juan Carlos
CORPORATE SOURCE: Facultad de Ciencias Quimicas, Centro de Quimica del Instituto de Ciencias, Benemerita Universidad Autonoma de Puebla, Puebla de Zaragoza, 72570, Mex.
SOURCE: THEOCHEM (2005), 728(1-3), 7-13
CODEN: THEODJ; ISSN: 0166-1280
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 14α-Demethylation is the reaction which leads directly to norlanosterol from lanosterol, and is carried out exclusively by lanosterol structure. To discover the features which make lanosterol a unique mol. able to undergo this demethylation, the electronic and energetic parameters of lanosterol and other structurally related steroids, were calcd. Local and global parameters were analyzed, in order to insight into the reactivity and selectivity of every mol. studied. Electrostatic potential maps were used to find differences of selectivity in each mol., along with total energy and hardness, discovering the differences in reactivity. Lanosterol shows specific orientation and unique shape of electrostatic potential map, which does not appear in other structures, except epilanosterol, because it differs only in the orientation of a hydroxyl group, therefore they present many similarities but many differences also. For this reason, epilanosterol has a similar shape of electrostatic potential map, but not its orientation. Aoyama et al. have found, three essential structural features in lanosterol to be demethylated, which generate a specific electrostatic potential map, the hydroxyl group on C-3, the position of the double bound between C8 and C9 on cycle B, and the side chain double bond. Our study agrees with some biochem. studies, which reveal that there are three key features essential for substrate recognition by the enzyme P 45014DM. We think the present study is an alternative methodol. to find features which are related with some parameters obtained via theor. calcns.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 13 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2004:161160 CAPLUS
DOCUMENT NUMBER: 140:300853
TITLE: A functional cytochrome P450 lanosterol 14α-demethylase CYP51 enzyme in the acrosome: Transport through the golgi and synthesis of meiosis-activating sterols
AUTHOR(S): Cotman, M.; Jezek, D.; Tacer, K. Fon; Frangez, R.; Rozman, D.
CORPORATE SOURCE: Laboratory for Genetics, Veterinary Faculty, University of Ljubljana, Ljubljana, SI-1000, Slovenia
SOURCE: Endocrinology (2004), 145(3), 1419-1426
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mammalian lanosterol 14α-demethylase (CYP51) is a microsomal cytochrome P 450 that demethylates lanosterol to FF-MAS, an oocyte meiosis-activating sterol and late intermediate of cholesterol biosynthesis. Herein the authors report CYP51 unequivocally localized to acrosomal membranes of male germ cells in mouse, bull, and ram, in which it synthesizes FF-MAS in the presence of the acrosomal form of NADP reduced-P 450 reductase. In the mouse, CYP51 (53 kDa) resides in endoplasmic reticulum (ER) and Golgi during all phases of acrosome development, indicating an intracellular transport from ERs through the Golgi to the acrosome. CYP51 (50 kDa) also resides on acrosomal membranes of bull- and ram-ejaculated sperm. In mouse liver, a 53-kDa CYP51 is no longer detected in trans Golgi, suggesting retrieval back to the ER and no further transport to other organelles. Glycosylated high-mol.-mass CYP51-immunoreactive proteins in acrosomal membranes of bull and ram and Golgi-enriched fractions of mouse liver indicate that mammalian CYP51s are subjected to post-translational modifications in the Golgi. In conclusion, CYP51 is the first cytochrome P 450 enzyme to be detected on acrosomal membranes. It exhibits a unique, cell-type-specific intracellular transport that is in agreement with its cell-type-specific physiol. role: prodn. of cholesterol in the liver and sterols with signaling properties in sperm. Demethylation of lanosterol to FF-MAS by the acrosomal lanosterol 14α-demethylase enzyme complex demonstrates for the first time the ability of ejaculate sperm to synthesize meiosis-activating sterols.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2003:996245 CAPLUS
DOCUMENT NUMBER: 140:159577
TITLE: Sterol Methyltransferase: Functional Analysis of Highly Conserved Residues by Site-Directed Mutagenesis
AUTHOR(S): Nes, W. David; Jayasimha, Pruthvi; Zhou, Wenxu; Kanagasabai, Ragu; Jin, Changxiao; Jaradat, Tahhan T.; Shaw, Robert W.; Bujnicki, Janusz M.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, TX, 79409-1061, USA
SOURCE: Biochemistry (2004), 43(2), 569-576
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sterol methyltransferase (SMT), the enzyme from Saccharomyces cerevisiae that catalyzes the conversion of sterol acceptor in the presence of AdoMet to C-24 methylated sterol and AdoHcy, was analyzed for amino acid residues that contribute to C-methylation activity. Site-directed mutagenesis of nine aspartate or glutamate residues and four histidine residues to leucine (amino acids highly conserved in 16 different species) and expression of the resulting mutant proteins in Escherichia coli revealed that residues at H90, Asp-125, Asp-152, Glu-195, and Asp-276 are essential for catalytic activity. Each of the catalytically impaired mutants bound sterol, AdoMet, and 25-azalanosterol, a high energy intermediate analog inhibitor of C-methylation activity. Changes in equil. binding and kinetic properties of the mutant enzymes indicated that residues required for catalytic activity are also involved in inhibitor binding. Anal. of the pH dependence of log kcat/Km for the wild-type SMT indicated a pH optimum for activity between 6 and 9. These results and data showing that only the mutant H90L binds sterol, AdoMet, and inhibitor to similar levels as the wild-type enzyme suggest that H90 may act as an acceptor in the coupled methylation-deprotonation reaction. CD spectra and chromatog. information of the wild-type and mutant enzymes confirmed retention of the overall conformation of the enzyme during the various expts. Taken together, the authors' studies suggest that the SMT active center is composed of a set of acidic amino acids at positions 125, 152, 195, and 276, which contribute to initial binding of sterol and AdoMet and that the H90 residue functions subsequently in the reaction progress to promote product formation.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2003:881353 CAPLUS
DOCUMENT NUMBER: 140:317052
TITLE: Sterol methyltransferase2: purification, properties, and inhibition
AUTHOR(S): Zhou, Wenxu; Nes, W. David
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, TX, 79409-1061, USA
SOURCE: Archives of Biochemistry and Biophysics (2003),

420(1), 18-34
CODEN: ABBIA4; ISSN: 0003-9861
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Expression of the Arabidopsis sterol methyltransferase2 (SMT2) cDNA in Escherichia coli yields a native protein, when purified to homogeneity, has the predicted mol. mass ~40 kDa on SDS-PAGE and recognizes native sterols synthesized by Arabidopsis with a Δ24(25)-bond (cycloartenol; Km 35 μM and kcat 0.001 s-1) and Δ24(28)-bond (24(28)-methylenelophenol; Km 28μM and kcat 0.01 s-1). Cycloartenol was converted to a single olefinic product-24(28)-methylenecycloartanol whereas 24(28)-methylenelophenol was converted to a mixt. of three stereochem. related products with the Δ24(28)Z-ethylidene, Δ24(28)E-ethylidene, and Δ25(27)-24β-Et side chains. Structural determinants essential to activity were the nucleophilic features at C-3 and C-24. The double bond position in the sterol substrate influenced catalytic efficiency according to the order: side chain, Δ24(24)<Δ24(28) and nucleus, Δ7<Δ8<Δ5=9,19-cyclopropane. The 14α-Me group was harmful to catalysis, reducing the suitability of cycloartenol as a substrate. On the basis of substrate activity and product distribution, SMT action was probed further using substrate (26,27-dehydroxymosterol; 26,27-DHZ) and intermediate (25-azacycloartenol: 25-AC) analogs of the SMT-catalyzed reactions. 26,27-DHZ was C-methylated to 26-homocholesta-8(9), 23(24)E, 26(26')-trienol as well as 26-homocholesta-8(9),26(26')-3β,24β-dienol by SMT2, Km of 15 μM, kcat of 0.001 s-1. In addn., 26,27-DHZ acted as a mechanism-based irreversible inhibitor that results in the specific covalent modification of SMT2, exhibiting Ki of 49 μM, kinact of 0.009 s-1 and partition ratio of 0.11. Substrate protection with zymosterol, 24(28)-methylenelophenol against 26,27-DHZ and similar inhibition of the first and second C1-transfer activities by the reversible inhibitor 25-AC of Ki 20 nM suggested that analogs interacted at the same active site. [28E-2H]- and [28Z-2H]24(28)-methylenelanosterols were paired with AdoMet and differences of 2H-incorporation in the enzyme-generated 24-Et olefins supported an antimechanism. The results suggest plant SMT2 has a position-specific substrate specificity for Δ24(25)-sterols and contains a single active center to catalyze the consecutive C1-transfer activities by substrate reaction channels similar to the fungal SMT1.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 16 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2003:684951 CAPLUS
DOCUMENT NUMBER: 139:347424
TITLE: Biosynthesis of Phytosterols: Kinetic Mechanism for the Enzymatic C-Methylation of Sterols
AUTHOR(S): Nes, W. David; Song, Zhihong; Dennis, Allen L.; Zhou, Wenxu; Nam, Jaewook; Miller, Matthew B.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, TX, 79409-1061, USA
SOURCE: Journal of Biological Chemistry (2003), 278(36), 34505-34516
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cloned soybean sterol methyltransferase was purified from Escherichia coli to gel electrophoretic homogeneity. From initial velocity expts., catalytic consts. for substrates best suited for the first and second C1 transfer activities, cycloartenol and 24(28)-methylenelophenol, were 0.01 and 0.001 s-1, resp. The substrate kinetic anal. using cycloartenol and S-adenosyl-L-methionine (AdoMet) generated an intersecting line pattern characteristic of a ternary complex kinetic mechanism. The high energy intermediate analog 25-azacycloartanol was a noncompetitive inhibitor vs. cycloartenol and an uncompetitive inhibitor vs. AdoMet. The dead end inhibitor analog cyclolaudenol was competitive vs. cycloartenol and uncompetitive vs. AdoMet. 24(28)-Methylenecycloartanol and AdoHcy generated competitive and noncompetitive kinetic patterns, resp., with

respect to AdoMet. Therefore, 24(28)-methylenecycloartanol combines with the same enzyme form as does cycloartenol and must be released from the enzyme before AdoHcy. 25-Azacycloartanol inhibited the first and second C1 transfer activities with about equal efficacy (Ki = 45 nM), suggesting that the successive C-methylation of the Δ24 bond occurs at the same active center. Comparison of the initial velocity data using AdoMet vs. [2H3-methyl]AdoMet as substrates tested against satg. amts. of cycloartenol indicated an isotope effect on VCH3/VCD3 close to unity. [25-2H]24(28)-Methylenecycloartanol, [28E-2H]24 (28)-methylenelanosterol, and [28Z-2H]24(28)-methylene lanosterol were prepd. and paired with AdoMet or [methyl-3H3]AdoMet to examine the kinetic isotope effects attending the C-28 deprotonation in the enzymic synthesis of 24-ethylidene) sterols. The stereochem. features as well as the observation of isotopically sensitive branching during the second C-methylation suggests that the two methylation steps can proceed by a change in chem. mechanism resulting from differences in sterol structure, concerted vs. carbocation; the kinetic mechanism remains the same during the consecutive methylation of the Δ24 bond.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2002:486117 CAPLUS
DOCUMENT NUMBER: 137:42095
TITLE: Process to increase concentration of meiosis-activating sterols (MAS) in cholesterol synthesis using potent inhibitors of Δ24-redn. and/or 4α-demethylation
INVENTOR(S): Lindenthal, Bernhard
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: Eur. Pat. Appl., 31 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1216701	A1	20020626	EP 2000-250456	20001222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
WO 2002051393	A2	20020704	WO 2001-EP14982	20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: EP 2000-250456 A 20001222
AB The invention relates to a process of increasing the concn. of meiosis-activating sterols (MAS) in cholesterol synthesis using potent inhibitors of Δ24-redn. and/or 4α-demethylation. Pharmaceutical compns. comprising the potent inhibitors are also claimed. Since the MAS are responsible for the control of fertility the inhibitors can be used to treat infertility or as contraceptives. The inhibitors can also be used in the microbiol. prodn. of MAS. Progesterone, pregnenolone, 17α-hydroxypregnenolone, 17α-hydroxyprogesterone, 4-androsten-3,17-dione, testosterone, medroxyprogesterone, verapamil, tamoxifen, ursodeoxycholic acid, chenodeoxycholic acid, deoxycholic acid, lithocholic acid, cortisone, cortisol, 11-deoxycortisol, 17β-estradiol, aldosterone, dehydroepiandrosterone, norethynodrel, 11-deoxycorticosterone, corticosterone, 6-amino-2-n-pentylthiobenzothiazole or mixts. of them are claimed as inhibitors.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN

Full Text
ACCESSION NUMBER: 2002:377063 CAPLUS
DOCUMENT NUMBER: 137:197313
TITLE: Theoretical assessment of the mechanisms involved in the cholesterol biosynthesis from lanosterol
AUTHOR(S): Cabrera-Vivas, B. M.; Ramirez, J. C.; Martinez-Aguilera, L. M. R.; Kubli-Garfias, C.
CORPORATE SOURCE: Facultad de Ciencias Quimicas, Benemerita Universidad Autonoma de Puebla, Puebla de Zaragoza, 72530, Mex.
SOURCE: THEOCHEM (2002), 584, 5-18
CODEN: THEODJ; ISSN: 0166-1280
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A theor. approach to describe the mechanisms of the isomerization and redn. of a double bond, involved in the lanosterol conversion to cholesterol was undertaken. Also, the 14α-demethylation and 4α-demethylation in this biosynthesis were studied, and some similarities were found between the two; however they are different and their mechanisms have not been explained yet. Ab initio calcns. were performed in order to prove these mechanisms. Two different characteristics involved in this biosynthesis were explained, namely (i) the stability of each mol. during this reaction using total energy, hardness and dipole moment, and (ii) the explanation of proposed mechanisms [Steroid Biochem. and Pharmacol., 1970, p. 57] of the two different reactions, using frontier orbitals and at. charges. For this sequence of reactions, the hardness and dipole moment indicate the hydro-acidy. of the mols., which means that carrying properties change through cell membranes. It is possible to explain the reaction mechanisms using frontier MOs theory and the at. charge. The localization of HOMO, LUMO and the flow of at. charge are in agreement with reported mechanisms [Steroids 8 (1966) 353; Medicinal Natural Products, 1997, p. 218; Biochem. of Steroid Hormones, 1975, p. 1].
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 19 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2001:250802 CAPLUS
DOCUMENT NUMBER: 135:58272
TITLE: Ergosterol biosynthesis in novel melanized fungi from hypersaline environments
AUTHOR(S): Mejanelle, Laurence; Lopez, Jordi F.; Gunde-Cimerman, Nina; Grimalt, Joan O.
CORPORATE SOURCE: Department of Environmental Chemistry, I.C.E.R.-C.S.I.C., Barcelona, 08034, Spain
SOURCE: Journal of Lipid Research (2001), 42(3), 352-358
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Halotolerant and halophilic melanized fungi were recently described in hypersaline waters. A close study of the sterol compn. of such fungi, namely Hortaea werneckii, Alternaria alternata, Cladosporium sphaerospermum, Cladosporium sp., and Aureobasidium pullulans, revealed the dominance of ergosterol and the presence of 29 intermediates of its biosynthesis pathway. The presence or absence of intermediates from distinct synthesis routes gave insight into the operative synthetic pathways from 4,4,14-trimethylcholesta-8,24-dien-3β-ol (lanosterol) to ergosterol in melanized fungi and in Saccharomyces cerevisiae, a ref. yeast cultured in parallel. In all studied melanized fungi, initial methylation at C-24 took place before C-14 and C-4 demethylation, involving a different reaction sequence from that obsd. in S. cerevisiae. Further transformation was obsd. to occur through various routes. In A. alternata, isomerization at C-7 takes place prior to desatn. at C-5 and C-22, and methylene redn. at C-24. In addn. to these pathways in Cladosporium spp., H. werneckii, and A. pullulans, ergosterol may also be synthesized through redn. of the C-24 methylene group before desatn. at C-5 and C-22 or vice versa. Moreover, in all studied melanized fungi except A. alternata, ergosterol biosynthesis may also proceed through C-24 methylene redn. prior to C-4 demethylation.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 20 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2000:833929 CAPLUS
DOCUMENT NUMBER: 134:71757
TITLE: Ab initio calculations for elucidation of the lanosterol 14α-demethylation mechanism
AUTHOR(S): Cabrera-Vivas, B. M.; Melendez, F. J.; Martinez-Aguilera, L. M. R.; Kubli-Garfias, C.
CORPORATE SOURCE: Facultad de Ciencias Quimicas, Benemerita Universidad Autonoma de Puebla, Puebla de Zaragoza, Mex.
SOURCE: THEOCHEM (2000), 532, 245-256
CODEN: THEODJ; ISSN: 0166-1280
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ab initio calcns. at the RHF/6-31G* level were performed with the SPARTAN program in order to elucidate the best pathway through which norlanosterol could be biosynthesized from lanosterol (demethylation). Two possible main pathways have been reported: the pathway via intermediate carboxylic acid proposed by Olson and Akhtar, and the pathway via intermediate formyloxy proposed by Alexander et al. The formyloxy pathway is more feasible than the carboxylic acid pathway based on an anal. of frontier orbitals, hardness/softness and reactivity parameters.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 21 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 2000:395923 CAPLUS
DOCUMENT NUMBER: 133:189678
TITLE: Sterol C-methyl transferase from Prototheca wickerhamii mechanism, sterol specificity and inhibition
AUTHOR(S): Mangla, A. T.; Nes, W. D.
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, TX, 79409, USA
SOURCE: Bioorganic & Medicinal Chemistry (2000), 8(5), 925-936
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The membrane-bound sterol Me transferase (SMT) enzyme from Prototheca wickerhamii, a non-photosynthetic, yeast-like alga, was found to C-methylate appropriate Δ24(25)-sterol acceptor mols. to Δ25(27)-24β-Me products exclusively. Incubation with pairs of substrates-[2H3-methyl]AdoMet and cycloartenol, and AdoMet and [27-13C]lanosterol-followed by 1H and 13C NMR anal. of the isotopically labeled products demonstrated the si-face (β-face attack) mechanism of C-methylation and the regiospecificity of Δ25(27)-double bond formation from the pro-Z Me group (C27) on lanosterol. The enzyme has a substrate preference for a sterol with a 3β-hydroxyl group, a planar nucleus and a side chain oriented into a 'right-handed' structure (20R-chirality)-characteristic of the native substrate, cycloartenol. The apparent native mol. wt. of the SMT was detd. to be approx. 154,000, as measured by Superose 6 FPLC. A series of sterol analogs which contain heteroatoms substituted for C24 and C25 or related structural modifications, including a steroidal alkaloid, have been used to probe further the active site and mechanism of action of the SMT enzyme. Sterol side chains contg. isoelectronic modifications of a pos. charged moiety in the form of an ammonium group substituted for carbon at C25, C24, C23 or C22 are particularly potent non-competitive inhibitors (Ki for the most potent inhibitor tested, 25-azacycloartanol, was ca. 2 nM, four orders of magnitude less than the Km for cycloartenol of 28 μM), supporting the intermediacy of the 24-Me C24(25)-carbenium ion intermediate. Ergosterol, but neither cholesterol nor sitosterol, was found to inhibit SMT activity (Ki=80 μM). The combination of results suggests that the interrelationships of substrate functional groups within the active center of a Δ24(25) to Δ25(27)24β-methyl-SMT could be approximated thereby allowing the rational design of C-methylation inhibitors to be formulated and tested.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 22 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1999:109792 CAPLUS
DOCUMENT NUMBER: 130:308355
TITLE: Site-Directed Mutagenesis of the Sterol Methyl Transferase Active Site from Saccharomyces cerevisiae Results in Formation of Novel 24-Ethyl Sterols
AUTHOR(S): Nes, W. David; McCourt, Brian S.; Marshall, Julie A.; Ma, Jianzhong; Dennis, Allen L.; Lopez, Monica; Li, Haoxia; He, Ling
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, TX, 79409, USA
SOURCE: Journal of Organic Chemistry (1999), 64(5), 1535-1542
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Δ24(28)-Sterols are end products of a mono C-methylation pathway catalyzed by the native Δ24(25)- to Δ24(28)-sterol methyltransferase (SMT) enzyme from Saccharomyces cerevisiae. Using a Tyr81 to Phe mutant SMT enzyme of S. cerevisiae, generated by site-directed mutagenesis of a highly conserved residue in the sterol binding site, the authors found that several Δ24(25)- and Δ24(28)-sterols, which are not substrates for the native protein, were catalyzed to mono- and bis-C24-alkylated side chains. The mutant protein behaved similarly to the native protein in chromatog. and in binding zymosterol, the preferred substrate. Zymosterol was converted to fecosterol by the Y81F mutant protein with similar turnover efficiency as the native protein (Km = 12 μM and kcat = 0.01 s-1); trace 24-Et sterols were detected from these incubations. 4α-Me zymosterol, which is not a normal substrate for the wild-type SMT enzyme, was converted to 4α-Me fecosterol in high yield. When fecosterol and 4α-Me fecosterol were assayed individually at satg. concns. only fecosterol served as an effective substrate for the second C-transfer step (Km = 38 μM and kcat = 0.002 s-1), suggesting that successive C-methylation of Δ24(28)-substrates is limited by product release and that mol. recognition of sterol features involves hydrogen bond formation. Isomeric 24-Et sterol olefins generated from 24(28)-methylene cholesterol were characterized by chromatog. (GC and HPLC) and spectral methods (MS and 1H NMR), viz., fucosterol, isofucosterol, and clerosterol. Changes in rate of C-methylation and product distributions resulting from deuterium substitution at C28 were used to establish the kinetic isotope effects (KIEs) for the various deprotonations leading to C24-methylene, C24-ethylidene, and C24-Et sterols. An isotope effect on C28 Me deprotonation generated during the first C1-transfer was detected with zymosterol and desmosterol paired with AdoMet and [2H3-methyl]AdoMet. A similar expt. to test for a KIE generated during the second C1-transfer reaction with AdoMet paired with 24(28)-methylenecholesterol and [28-2H2]24(28)-methylene cholesterol indicated an inverse isotope effect assocd. with C27 deprotonation. Alteration in the proportion of the C24 alkylated olefinic products generated by the pure Y81F mutant resulted from the suppression of the formation of Δ24(28)-ethylidene sterols (C28 deprotonation) by a primary deuterium isotope effect with a compensating stimulation of the formation of 24-Et sterols (C27 deprotonation). Kinetic study on the rate of product formation indicated a normal KIE of kH/kD = 2.62 for the first C1-transfer. Alternatively, an inverse KIE was established with kH/kD = 0.9 for the second C1-transfer resulting from conversion of the 24(28)-double bond (Sp2 hybridization) to a 24β-Et group (Sp3 hybridization). From the structures and stereochem. assignments of the C-Et olefin products, the stereochem. of the attack of AdoMet in the second C1-transfer was found to operate a Si-face (backside) attack at C24, analogous to the first C1-transfer reaction..
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 23 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1998:326630 CAPLUS

DOCUMENT NUMBER: 129:76321
TITLE: Overexpression, purification, and stereochemical studies of the recombinant (S)-adenosyl-L-methionine:Δ24(25)-to Δ24(28)-sterol methyl transferase enzyme from Saccharomyces cerevisiae
AUTHOR(S): Nes, W. David; McCourt, Brian S.; Zhou, Wen-Xu; Ma, Jianzhong; Marshall, Julie A.; Peek, Lauri-Ann; Brennan, Michael
CORPORATE SOURCE: Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, TX, 79409, USA
SOURCE: Archives of Biochemistry and Biophysics (1998), 353(2), 297-311
CODEN: ABBIA4; ISSN: 0003-9861
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ERG6 gene that encodes (S)-adenosyl-L-methionine:Δ24(25)- to Δ24(28)-sterol Me transferase (SMT) enzyme from Saccharomyces cerevisiae was introduced into plasmid pET23a(+) and the resulting native protein was overexpressed in BL21(DE3) host cells under control of a T7 promoter. This enzyme was purified to apparent homogeneity by ammonium sulfate pptn., anion exchange, and hydrophobic interaction chromatog. N-Terminal sequence anal. of the first 10 amino acids of the purified SMT protein confirmed the identity of the start triplet and expected primary structure. The enzyme exhibited a turnover no. of 0.01/s and an isoelec. point of 5.95. A combination of Superose 6 chromatog. and sodium dodecyl sulfate-polyacrylamide gel electrophoresis showed that the purified SMT enzyme possessed a native mol. wt. of 172,000 and was tetrameric. The purified SMT enzyme generated kinetics in which velocity vs. substrate curves relative to zymosterol (preferred sterol acceptor mol.) and AdoMet were sigmoidal rather than hyperbolic, indicating enzyme cooperativity among the subunits. Studies on product formation using [27-13C]zymosterol and [2H3-methyl]AdoMet incubated with the pure SMT enzyme confirmed the reaction mechanism of sterol methylation to involve a 1,2-hydride shift of H-24 to C-25 from the Re-face of the original 24,25-double bond. Deduced amino acid sequence comparisons of the SMT polypeptide from S. cerevisiae with related sterol Me transferase enzymes of plant and fungal origin indicate that there is a significant degree of similarity between these enzymes. Specifically, there is a conserved sequence (in yeast from amino acids ca. 79 to 92 which contains an YXGHG motif; referred to as Region I) that is not present in other AdoMet-dependent Me transferase enzymes.
REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 24 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1998:246504 CAPLUS
DOCUMENT NUMBER: 129:39650
TITLE: Increased plasma, biliary, and hepatic cholesterol precursors in pigs with ileal autotransplantation-induced malabsorption of cholesterol and bile acids
AUTHOR(S): Pakarinen, M. P.; Halttunen, J.; Kuusanmaki, P.; Miettinen, T. A.
CORPORATE SOURCE: Second Dept. of Surgery and Second Dept. of Internal Medicine, Helsinki University Central Hospital, University of Helsinki, Helsinki, FIN 00290, Finland
SOURCE: Scandinavian Journal of Gastroenterology (1998), 33(3), 319-326
CODEN: SJGRA4; ISSN: 0036-5521
PUBLISHER: Scandinavian University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Small-bowel transplantation impairs intestinal absorptive function for unknown reasons. The proportions of plasma, biliary, and hepatic cholesterol precursors to cholesterol were detd. by gas-liq. chromatog. after resection of the proximal 75% of the porcine jejunoileum and autotransplantation of the remaining ileum and were related to in vivo absorption and fecal excretion of cholesterol. Ileal autotransplantation significantly decreased serum (18%) and liver (7.6%) cholesterol content, the esterification percentage of serum cholesterol (5.1%), and the total amt. of cholesterol absorbed (48%) and increased fecal excretion of bile

acids (108%), net cholesterol elimination (53%), and the proportions of plasma (207%), biliary (183%), and hepatic (114%) cholesterol precursors. The increases were most striking for the side-chain-satd. demethylated sterols, cholestanol and lathosterol, and monomethyl sterols, whose bile/liver and plasma/liver ratios were increased in the autotransplantation group. Plasma, biliary, and hepatic precursor proportions were pos. related to each other and similarly correlated with fecal bile acids and the net elimination of cholesterol in feces. These findings suggest that ileal autotransplantation in pigs with proximal gut resection increased the levels of cholesterol precursor sterols in plasma, bile, and liver mainly due to a bile-acid-malabsorption-induced increase in hepatic synthesis of cholesterol. Enhanced secretion of cholesterol precursors from the liver into the plasma and bile may have contributed to their increased values during the increased rate of cholesterogenesis.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 25 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1997:716588 CAPLUS
DOCUMENT NUMBER: 128:20441
TITLE: A new triazole, voriconazole (UK-109,496), blocks sterol biosynthesis in Candida albicans and Candida krusei
AUTHOR(S): Sanati, Homayoon; Belanger, Paul; Fratti, Rutilio; Ghannoum, Mahmoud
CORPORATE SOURCE: Division Infectious Diseases, Harbor-UCLA Medical Center, Torrance, CA, 90509, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1997), 41(11), 2492-2496
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Voriconazole (UK-109,496) is a novel triazole deriv. with potent broad-spectrum activity against various fungi, including some that are inherently resistant to fluconazole, such as Candida krusei. In this study, the authors compared the effect of subinhibitory concns. of voriconazole and fluconazole on sterol biosynthesis of fluconazole-resistant and -susceptible Candida albicans strains, as well as C. krusei, in an effort to delineate the precise mode of action of voriconazole. Voriconazole MICs ranged from 0.003 to 4 μg/mL, while fluconazole MICs ranged from 0.25 to >64 μg/mL. To investigate the effects of voriconazole and fluconazole on candidal sterols, yeast cells were grown in the absence and presence of antifungals. In untreated C. albicans controls, ergosterol was the major sterol (accounting for 53.6% ± 2.2% to 71.7% ± 7.8% of the total) in C. albicans and C. krusei strains. There was no significant difference between the sterol compns. of the fluconazole-susceptible and -resistant C. albicans isolates. Voriconazole treatment led to a decrease in the total sterol content of both C. albicans strains tested. In contrast, exposure to fluconazole did not result in a significant redn. in the total sterol content of the three candidal strains tested (P > 0.5). Gas-liq. chromatog. anal. revealed profound changes in the sterol profiles of both C. albicans strains and of C. krusei in response to voriconazole. This antifungal agent exerted a similar effect on the sterol coepns. of both fluconazole-susceptible and -resistant C. albicans strains. Interestingly, a complete inhibition of ergosterol synthesis and accumulation of its biosynthetic precursors were obsd. in both strains treated with voriconazole. In contrast, fluconazole partially inhibited ergosterol synthesis. Anal. of sterols obtained from a fluconazole-resistant C. albicans strain grown in the presence of different concns. of voriconazole showed that this agent inhibits ergosterol synthesis in a dose-dependent manner. In C. krusei, voriconazole significantly inhibited ergosterol synthesis (over 75% inhibition). C. krusei cells treated with voriconazole accumulated the following biosynthetic intermediates: squalene, 4,14-dimethylzymosterol, and 24-methylenedihydrolanosterol. Accumulation of these methylated sterols is consistent with the premise that this agent functions by inhibiting fungal P 450-dependent 14α-demethylase. As expected, treating C. krusei with fluconazole minimally inhibited ergosterol synthesis. Importantly, our data indicate that voriconazole is more effective than fluconazole in blocking candidal sterol biosynthesis,

consistent with the different antifungal potencies of these compds.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 26 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1997:625148 CAPLUS
DOCUMENT NUMBER: 127:316142
TITLE: Cholesterol biosynthesis from lanosterol: development of a novel assay method and characterization of rat liver microsomal lanosterol Δ24-reductase
AUTHOR(S): Bae, Soo-Han; Paik, Young-Ki
CORPORATE SOURCE: Department of Biochemistry and Bioproducts Research Center, College of Science, Yonsei University, Seoul, 120-749, S. Korea
SOURCE: Biochemical Journal (1997), 326(2), 609-616
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The membrane-bound sterol Δ24-reductase (24-reductase) catalyzes anaerobic redn. of 24(25)-enes of lanosterol and other obligatory intermediates of cholesterol biosynthesis from lanosterol. A novel assay method and properties of the 24-reductase are described. More than a 120-fold induction of the 24-reductase activity was achieved by feeding rats a diet contg. 5% cholestyramine plus 0.1% lovastatin in chow and by modulating diurnal variation. With this enzyme induction condition, lanosterol was converted efficiently into dihydrolanosterol in both intact hepatic microsomes and freshly isolated hepatocytes only when either miconazole or CO was added to inhibit 14α-demethylation of lanosterol. AR45 cells, which are deficient in 14α-Me demethylase (14α-DM), exhibit lanosterol 24-reductase activity without addn. of either CO or miconazole. Conversely, inhibition of the 24-reductase was not required for the expression of 14α-DM activity. Studies on the substrate specificities for the 24-reductase using different 24(25)-enes showed that the most reactive substrate was 5α-cholesta-7,24-dien-3β-ol, which exhibited a maximal 18-fold higher kcat than that of lanosterol without the aid of the 14α-DM inhibitor. In addn., both the kinetic behavior of lanosterol substrate in relation to the 24-reductase and a non-competitive inhibition mode of U18666A (KI 0.157 μM) as well as Tripanaxol (KI 0.23 μM), two well-known 24-reductase inhibitors, were detd. On the basis of our new findings on the preferred substrate and on the neg. effect of 14α-DM on the 24-reductase, we suggest that C-24 redn. of sterols takes place straight after sterol Δ8→7 isomerization of zymosterol, which occurs several steps after C-32 demethylation of lanosterol in the 19-step pathway of cholesterol biosynthesis from lanosterol.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 27 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1997:584623 CAPLUS
DOCUMENT NUMBER: 127:289786
TITLE: Stereochemical features of C-methylations on the path to Δ24(28)-methylene and Δ24(28)-ethylidene sterols: studies on the recombinant phytosterol methyl transferase from Arabidopsis thaliana
AUTHOR(S): Tong, Yusen; McCourt, Brian S.; Guo, De-an; Mangla, Anil T.; Zhou, Wen-Xu; Jenkins, Mark D.; Zhou, Wen; Lopez, Monica; Nes, W. David
CORPORATE SOURCE: Dep. Chemistry and Biochemistry, Texas Tech Univ., Lubbock, TX, 79409, USA
SOURCE: Tetrahedron Letters (1997), 38(35), 6115-6118
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Using a homogenate prepd. from Escherichia coli cells that express the sterol Me transferase (SMT) gene of Arabidopsis thaliana, migration of the hydrogen atom at C-24 to C-25 from the Re-face of the double bond was

demonstrated in the biosynthesis of [27-13C] 24(28)-methylenezymosterol (fecosterol) from [27-13C]zymosterol and the chirality of the C-25 stereocenter (2SR) was retained after the stereospecific conversion of [27-13C]24(28)-methylenezymosterol to [27-13C](24(28)Z)-ethylidenecholest-8-en-3β-ol.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 28 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1997:386722 CAPLUS
DOCUMENT NUMBER: 127:118927
TITLE: Identification of cDNAs encoding sterol methyl-transferases involved in the second methylation step of plant sterol biosynthesis
AUTHOR(S): Bouvier-Nave, Pierrette; Husselstein, Tania; Desprez, Thierry; Benveniste, Pierre
CORPORATE SOURCE: Institut Biologie Moleculaire Plantes, Departement Enzymologie Cellulaire Moleculaire, Institut Botanique, Strasbourg, F-67083, Fr.
SOURCE: European Journal of Biochemistry (1997), 246(2), 518-529
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two Me transfers are involved in the course of plant sterol biosynthesis and responsible for the formation of 24-alkyl sterols (mainly 24-Et sterols) which play major roles in plant growth and development. The first Me transfer applies to cycloartenol, the second one to 24-methylene lophenol. Five cDNA clones encoding two Arabidopsis thaliana, two Nicotiana tabacum and one Ricinus communis S-adenosyl-L-methionine (AdoMet) sterol methyltransferases (SMT) were isolated. The deduced amino acid sequences of A. thaliana and N.tabacum SMT are about 80% identical in all possible combinations. In contrast they are about 40% identical with the deduced amino acid sequence of R. communis SMT and the published Glycine max sequence. Both A. thaliana and one N. tabacum SMT cDNAs were expressed in a yeast null mutant erg6, deficient in AdoMet zymosterol C24-methyltransferase and contg. C24-non-alkylated sterols. In all cases, several 24-ethylidene sterols were synthesized. A thorough study of the sterolic compn. of yeast expressing the A. thaliana cDNA 411 (erg6-411B-pYeDP60) showed 24-methylene and 24-ethylidene deriva. of 4-desmethyl, 4α-Me and 4,4-di-Me sterols as well as 24-Me and 24-Et derivs. of 4-desmethyl sterols. The structure of 5α-stigmasta-8, Z-24(24')-dien-3β-ol, the major sterol of transformed yeasts, was demonstrated by 400 MHz 1H NMR. Microsomes from erg6-411B-pYeDP60 were shown to possess AdoMet-dependent sterol-C-methyl-transferase activity. Delipidated prepns. of these microsomes converted cycloartenol into 24-methyllene cycloartanol and 24-methylene lophenol into 24-ethylidene lophenol, thus allowing the first identification of a plant sterol-C-methyltransferase cDNA. The catalytic efficiency of the expressed SMT was 17-times higher with 24-methylene lophenol than with cycloartenol. This result provides evidence that the A. thaliana cDNA 411 (and most probably the 3 plant SMT cDNAs presenting 80% identity with it) encodes a 24-methylene lophenol-C-241 methyltransferase catalyzing the second methylation step of plant sterol biosynthesis.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 29 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1997:347381 CAPLUS
DOCUMENT NUMBER: 127:77765
TITLE: Substrate-based inhibitors of the (S)-adenosyl-L-methionine: Δ24(25)- to Δ24(28)-sterol methyltransferase from Saccharomyces cerevisiae
AUTHOR(S): Nes, W. David; Guo, De-an; Zhou, Wen
CORPORATE SOURCE: Dep. Chem. Biochemistry, Texas Tech Univ., Lubbock, TX, 79409, USA
SOURCE: Archives of Biochemistry and Biophysics (1997), 342(1), 68-81
CODEN: ABBIA4; ISSN: 0003-9861

PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of 31 side-chain-modified analogs of cholesterol, zymosterol, lanosterol, and cycloartenol and the steroidal alkaloids solasodine and solanidine were studied as inhibitors of (S)-adenosyl-L-methionine:Δ24(25)-sterol methyltransferase (SMT) enzyme activity from Saccharomyces cerevisiae. Two classes of sterol methylation inhibitors were tested: substrate analogs, including mechanism-based inhibitors, and transition state analogs. Several novel sterol methylation inhibitors that contained an aza, aziridine, or ammonium group in the sterol side chain were prepd. and tested for the first time. The degree and kinetic pattern of methylation inhibition were influenced by the position and nature of the variant functional group introduced into the side chain. The most potent inhibitors of SMT enzyme activity were transition state analog inhibitors (Ki values of 5-10 nM) that mimicked the structure and conformation of the natural substrate presumed to form in the ternary complex generated in the transition state. Steroidal alkaloids were potent competitive inhibitors with Ki values ranging from 2-30 μM, which is about the Kmapp of zymosterol, ~27 μM. An isosteric analog of the natural substrate, zymosterol, in which the 26/27-gem-dimethyl groups were joined to form a cyclopropylidene function is shown to be a potent irreversible mechanism-based inactivator of SMT enzyme activity that exhibits competitive-type inhibition, Ki 48 μM with a Kinact of 1.52 min-1. Mechanistic implications of these results provide new insights into the topol. of the ternary complex involving sterol-AdoMet-enzyme.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 30 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1992:546829 CAPLUS
DOCUMENT NUMBER: 117:146829
TITLE: Sterol content of Candida maltosa strains with high resistance to nystatin
AUTHOR(S): Durasova, E. N.; Mikhailova, N. P.; Zhakovskaya, Z. A.; V'yunov, K. A.
CORPORATE SOURCE: NPO "Gidrolizprom", Russia
SOURCE: Mikologiya i Fitopatologiya (1991), 25(6), 487-92
CODEN: MIFIB2; ISSN: 0026-3648
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Nystatin-resistant mutants of C. maltosa were blocked in different stages of ergosterol synthesis: C24-transmethylation, Δ8-Δ7-isomerization, and 14α-demethylation. The mutants may be used to study biosynthetic pathways of sterols.

L8 ANSWER 31 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1992:17649 CAPLUS
DOCUMENT NUMBER: 116:17649
TITLE: Steric requirements for transformation of substrates by the (S)-adenosyl-L-methionine:Δ24(25)-sterol methyl transferase
AUTHOR(S): Nes, W. David; Janssen, Giselle G.; Bergenstrahle, Annika
CORPORATE SOURCE: Plant Fungal Lipid Res. Microb. Prod. Res. Unit, Richard B. Russell Res. Cent., Athens, GA, 30613, USA
SOURCE: Journal of Biological Chemistry (1991), 266(23), 15202-12
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The membrane-bound enzyme of microsomes obtained from sunflower embryos that catalyzes the biosubstrate transfer reaction whereby the Me group of (S)-adenosyl-L-methionine is transferred to C-24 of the sterol side chain was investigated. Optimal incubation conditions for assay of the microsomal (S)-adenosyl-L-methionine:sterol Δ24-Me transferase (SMT) have been established for the first time. The microsomal prepn catalyzed the formation of a Δ24(28)-sterol and was free of contaminating Me transferase enzymes, e.g. those which form Δ23-24 Me sterols

(cyclosadol) and Δ25-24β-Me sterols (cyclolaudenol) and other sterolic enzymes which might transform the acceptor mol. to metabolites which could compete in the assay with the test substrate. From a series of incubations with 27 sterol and sterol-like (triterpenoids) substrates of which 23 compds. possessed a 24,25-double bond, a marked dependence on precise structural features and three-dimensional shape of the acceptor mol. in its ability to be transformed by the SMT was obsd. In contrast to the yeast SMT where cycloartenol fails to bind to the SMT and zymosterol is the best substrate for methylation, the sunflower SMT studied here utilizes cycloartenol preferentially to zymosterol and the other substrates. Of the chem. groups which distinguishes cycloartenol, a free 3β-OH, 9β,19-cyclopropyl group, trimethylated acid. nucleus, and Δ24-double bond, only the nucleophilic centers at C-3 and C-24 were obligatory for substrate binding and methylation. Of the bent or flat conformations which cycloartenol may orient in the enzyme-substrate complex, the results indicate a selection for acceptor mols. which possess the shape that closely resembles the crystal state and soln. orientation of cycloartenol which is now known to be flat rather than bent.

L8 ANSWER 32 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1991:651948 CAPLUS
DOCUMENT NUMBER: 115:251948
TITLE: Sterol composition of nystatin-resistant Candida maltosa mutants
AUTHOR(S): Mikhailova, N. P.; Sorokoletova, E. F.; Durasova, E. N.; V'yunov, K. A.; Shapovalov, O. I.
CORPORATE SOURCE: All-Union Inst. Plant Mater. Hydrol., Leningrad, 198 099, USSR
SOURCE: Folia Microbiologica (Prague, Czech Republic) (1991), 36(2), 148-52
CODEN: FOMIAZ; ISSN: 0015-5632
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The compn. of sterol fractions of nystatin-resistant Candida maltosa strains was detd. Using UV-spectrometry, TLC, and GLC-MS it was demonstrated that resistance to nystatin is connected with the compn. alterations of yeast cell sterols. Block of different stages of ergosterol biosynthesis was revealed in some mutants, viz. C-24-transmethylation, Δ8 → Δ7-isomerization, 14α-demethylation, C-5(6)-dehydrogenation, redn. of C-14(15) and C-24(28) double bonds.

L8 ANSWER 33 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1988:106000 CAPLUS
DOCUMENT NUMBER: 108:106000
TITLE: Effects of ketoconazole on cholesterol synthesis and precursor concentrations in the rat liver
AUTHOR(S): Strandberg, Timo E.; Tilvis, Reijo S.; Miettinen, Tatu A.
CORPORATE SOURCE: Second Dep. Med., Univ. Helsinki, Helsinki, SF-00290, Finland
SOURCE: Lipids (1987), 22(12), 1020-4
CODEN: LPDSAP; ISSN: 0024-4201
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ketoconazole, an antimycotic agent, given to rats for 1 wk as a 0.05% food addn. had no effect on the hepatic concns. of free and esterified cholesterol or on the activity of Acyl CoA:cholesterol-acyltransferase (ACAT). However, the levels of free methylated cholesterol precursors, esp. lanosterols, less markedly Δ8,24 and Δ8-diMe sterols and monoMe sterols, were increased after 1 day's treatment, whereas those of esterified Me sterols were increased inconsistently, and those of free and esterified Δ8-lathosterol, lathosterol, and desmosterol were not affected. Cholestyramine treatment had no effect on ACAT in spite of a decrease in the hepatic content of esterified cholesterol and caused a marked increase in the free cholesterol precursor levels, esp. in those of lathosterols. Cholestyramine given to ketoconazole-treated rats increased the hepatic levels of Δ8- and Δ7-lathosterols but not desmosterol or methylated cholesterol precursors. Ketoconazole increased and cholestyramine markedly decreased plant sterols, sitosterol

and campesterol in the liver. In serum, the contents of both lanosterols and lathosterol were increased but that of cholesterol tended to be decreased by ketoconazole (-19%). Apparently, ketoconazole impairs demethylation processes at C-14 and to some extent at C-4 in the rat liver, resulting in lowered serum cholesterol level.

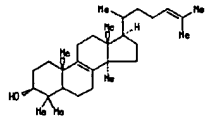
L8 ANSWER 34 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1988:87891 CAPLUS
DOCUMENT NUMBER: 108:87891
TITLE: Cholesterol metabolism during ketoconazole treatment in man
AUTHOR(S): Miettinen, Tatu A.
CORPORATE SOURCE: 2nd Dep. Med., Univ. Helsinki, Helsinki, SF-00290, Finland
SOURCE: Journal of Lipid Research (1988), 29(1), 43-51
CODEN: JLPRAW; ISSN: 0022-2275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ketoconazole, an antifungal antibiotic, inhibits cholesterol synthesis by blocking demethylation of lanosterol. Effects of this inhibition were studied on serum cholesterol, lipoproteins and cholesterol precursors, biliary lipid compn., and fecal steroid elimination in 5 patients with prostate cancer treated with large doses of ketoconazole. The serum level of total cholesterol fell by 27%, that of low-d. lipoprotein (LDL) cholesterol by 41% and that of low-d. apolipoprotein-B (LDL apoB) by 32% with ketoconazole alone; the fall in the total cholesterol level of a patient treated with ketoconazole-cholestyramine was 65%. Serum contents of free lanosterol and dihydrolanosterol increased up to 250 times, yet the total concns. remained <2 mg/dL. Of the other cholesterol precursor sterols only those with Δ8-double bond increased several fold, indicating that in addn. to 14α-demethylation, ketoconazole also interfered with metab. of later intermediary sterols to some extent. Compared with serum sterols, lanosterols were enriched in biliary and fecal sterols up to 10-20 times. Fecal lanosterol output increased from 12 to 247 mg/day, and comprised over 20% fecal steroids of endogenous origin. Bile acid synthesis was decreased, the proportion of chenodeoxycholic acid being markedly reduced in both biliary and fecal bile acids. Cholesterol absorption appeared to decrease yet fecal neutral sterol output and cholesterol synthesis were unchanged and the overall sterol synthesis was increased. Thus, ketoconazole inhibits cholesterol elimination as bile acids. However, by blocking 14α-demethylation, it results in effective drainage of sterol nucleus as lanosterols into bile and feces, which, in turn, is assocd. with a marked redn. in LDL cholesterol level probably through activation of hepatic LDL apoB receptors.

L8 ANSWER 35 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1987:15011 CAPLUS
DOCUMENT NUMBER: 106:15011
TITLE: The distinction of different types of cytochromes P-450 from the yeasts Candida tropicalis and Saccharomyces uvarum
AUTHOR(S): Sanglard, D.; Kaeppeli, O.; Fiechter, A.
CORPORATE SOURCE: Dep. Microbiol. Mol. Genet., Univ. Cincinnati, Cincinnati, OH, 45267, USA
SOURCE: Archives of Biochemistry and Biophysics (1986), 251(1), 276-86
CODEN: ABBIA4; ISSN: 0003-9861
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The distinction between 2 types of cytochromes P 450 originating from microsomes of C. tropicalis grown on glucose and on alkane was achieved. Criteria of differentiation between these 2 cytochrome P 450 forms were based on the characteristics of reduced CO difference spectra, on substrate specificity, and on binding and inhibition kinetics of the fungistatic compd. propiconazole. One cytochrome P 450 form catalyzed the 14α-demethylation of lanosterol and bound propiconazole with an equimolar ratio. This form was present in microsomes from glucose-grown cells and shared similar characteristics with the cytochrome P 450 of S. uvarum grown on the same C source. The other cytochrome P 450 form

catalyzed the terminal hydroxylation of aliph. hydrocarbons and showed a less specific binding ratio with propiconazole.(10) mol propiconazole/mol cytochrome P 450). This type of cytochrome P 450 was only present in the microsomes of C. tropicalis grown on alkane.

L6 ANSWER 36 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1986:163785 CAPLUS
DOCUMENT NUMBER: 104:163785
TITLE: Oxidative demethylation of lanosterol in cholesterol biosynthesis: accumulation of sterol intermediates
AUTHOR(S): Shafiee, Ali; Trzaskos, James M.; Paik, Young Ki; Gaylor, James L.
CORPORATE SOURCE: Cent. Res. Dev. Dep., E. I. du Pont de Nemours and Co., Wilmington, DE, 19898, USA
SOURCE: Journal of Lipid Research (1986), 27(1), 1-10
CODEN: JLPRAW; ISSN: 0022-2275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB With [24,25-3H]dihydrolanosterol as substrate, large-scale metabolic formation of intermediates of lanosterol demethylation by microsomes was carried out to identify all compds. in the metabolic process. By utilizing knowledge of electron transport of lanosterol demethylation, the demethylation reaction was interrupted, allowing accumulation and confirmation of the structure of the oxygenated intermediates lanost-8-en-3β,32-diol and 3β-hydroxylanost-8-en-32-al, as well as the demethylation product 4,4-dimethylcholesta-8,14-dien-3β-ol. Further metab. of the Δ8,14-diene intermediate to a single product, 4,4-dimethylcholest-8-en-3β-ol, occurs under interruption conditions in the presence of 0.5 mM CN-. With authentic compds., each intermediate was rigorously characterized by HPLC and gas-liq. chromatog. plus mass spectral anal. of isolated and derivatized sterols. Intermediates that accumulated in further abundance were further characterized by UV, 1H NMR, and IR spectroscopy of the isolated sterols.

L6 ANSWER 37 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1986:145250 CAPLUS
DOCUMENT NUMBER: 104:145250
TITLE: Evidence for the contribution of a sterol 14-reductase to the 14α-demethylation of lanosterol by yeast
AUTHOR(S): Aoyama, Yuri; Yoshida, Yuzo
CORPORATE SOURCE: Fac. Pharm. Sci., Mukogawa Women's Univ., Hyogo, 663, Japan
SOURCE: Biochemical and Biophysical Research Communications (1986), 134(2), 659-63
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Lanosterol (I) was converted to a 14-demethylated metabolite, 4,4-dimethylzymosterol by Saccharomyces cerevisiae microsomes. This metab. was mediated by a cytochrome P 450 (P 450/14DM). However, a reconstituted system consisting of P 450/14DM and its reductase converted lanosterol to the 14-desatd. deriv. of 4,4-dimethylzymosterol, 4,4-dimethyl-5α-cholesta-8,14,24-trien-3β-ol (trienol). When AY-9944 was added to the reaction system with the microsomes, the trienol

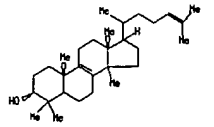
was formed with corresponding decrease in 4,4-dimethylzymosterol. Evidently, the 14α-demethylation of lanosterol by yeast microsomes occurs sequentially via the trienol. Redn. of the trienol to 4,4-dimethylzymosterol is mediated by an AY-9944-sensitive reductase.

L6 ANSWER 38 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1981:117494 CAPLUS
DOCUMENT NUMBER: 94:117494
TITLE: Inhibition of sterol transmethylation by S-adenosylhomocysteine analogs
AUTHOR(S): McCammon, Mark T.; Parks, L. W.
CORPORATE SOURCE: Dep. Microbiol., Oregon State Univ., Corvallis, OR, 97331, USA
SOURCE: Journal of Bacteriology (1981), 145(1), 106-12
CODEN: JOBAAY; ISSN: 0021-9193
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Structural analogs of S-adenosylhomocysteine were tested in vitro for inhibition of the yeast S-adenosylmethionine:Δ24-sterol-C-methyltransferase enzyme. These compds. exhibited a wide inhibitory range which suggested structural features of the parent compd. important in binding to the enzyme. No analog tested specifically inhibited only this enzyme. The most active compd. was sinefungin, which also inhibited growth of yeast cultures. Sterol exts. of cells grown in the presence of sinefungin revealed a dramatic increase in the levels of zymosterol, the sterol substrate in the transmethylation studied, and a concomitant decrease in the levels of ergosterol. Sinefungin was apparently transported into the cell by the same permease as S-adenosylmethionine. There it blocks the in vivo methylation of sterols in yeast.

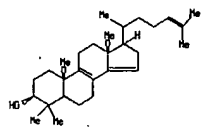
L6 ANSWER 39 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1981:80012 CAPLUS
DOCUMENT NUMBER: 94:80012
TITLE: Involvement of cytochrome b5 and a cyanide-sensitive monooxygenase in the 4-demethylation of 4,4-dimethylzymosterol by yeast microsomes
AUTHOR(S): Aoyama, Yuri; Yoshida, Yuzo; Sato, Ryo; Susani, Markus; Ruis, Helmut
CORPORATE SOURCE: Fac. Pharm. Sci., Mukogawa Univ., Hyogo, 663, Japan
SOURCE: Biochimica et Biophysica Acta, Lipids and Lipid Metabolism (1981), 663(1), 194-202
CODEN: BBLLA6; ISSN: 0005-2760
DOCUMENT TYPE: Journal
LANGUAGE: English
AB According to Ohba et al. (1978), yeast microsomes catalyze the removal of 3 Me groups attached to the C-4 and C-14 positions of lanosterol-1,7,15,22,26,30-14C (4,4,14α-trimethyl-5α-cholesta-8,24-dien-3β-ol) in the presence of NADPH, NAD+, and O2, concomitant with the liberation of 14CO2 derived from C-30 (1 of the 2 Me groups at the C-4 position). Here the 14CO2 formation from the 14C-labeled lanosterol was inhibited by antibodies to yeast cytochrome b5 and by palmitoyl-CoA, a substrate of the cytochrome b5-contg. fatty acyl-CoA desaturase system of yeast microsomes. However, neither the antibodies nor palmitoyl-CoA inhibited the conversion of lanosterol to 4,4-di-Me zymosterol (4,4-dimethyl-5α-cholesta-8,24-dien-3β-ol). Evidently cytochrome b5 and a CN--sensitive enzyme are involved in the 4-demethylation of 4,4-dimethylzymosterol, but not the 14α-demethylation of lanosterol, by yeast microsomes. A CN--sensitive enzyme apparently acts as the terminal 4-demethylase and cytochrome b5 transfers reducing equiv. from NADPH to the terminal enzyme, as in the case of fatty acyl-CoA desatn.

L6 ANSWER 40 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1980:510483 CAPLUS
DOCUMENT NUMBER: 93:110483
TITLE: Cytochrome P-450-containing monooxygenase system of yeast microsomes. Properties and role in sterol biosynthesis
AUTHOR(S): Yoshida, Yuzo; Aoyama, Yuri

CORPORATE SOURCE: Fac. Pharm. Sci., Mukogawa Univ., Nishinomiya, Japan
SOURCE: Microsomes, Drug Oxid., Chem. Carcinog., [Int. Symp. Microsomes Drug Oxid.], 4th (1980), Meeting Date 1979, Volume 2, 761-4. Editor(s): Coon, Minor Jesser; Conney, Allan H.; Estabrook, Ronald W. Academic: New York, N. Y.
CODEN: 43VMAC
DOCUMENT TYPE: Conference
LANGUAGE: English
GI



I



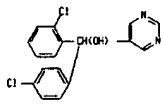
II

AB The cytochrome P-450 and NADPH-cytochrome P-450 reductase of Saccharomyces cerevisiae microsomes are characterized. A reconstituted cytochrome P-450-contg. electron transport system metabolized lanosterol (I) to a product which had physicochem. properties similar to those of 14-demethyllanosterol (II). A proposed scheme is presented for the 14α-demethylation of I. Evidently, the yeast cytochrome P-450 can catalyze the 3 oxygenations included in the 14α-demethylation of I.

L6 ANSWER 41 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1979:435480 CAPLUS
DOCUMENT NUMBER: 91:35480
TITLE: Studies on Δ8-Δ7 isomerization and methyl transfer of sterols in ergosterol biosynthesis of yeast
AUTHOR(S): Yabusaki, Yoshiyasu; Nishino, Tokuzo; Ariga, Nakao; Katsuki, Hirohiko
CORPORATE SOURCE: Fac. Sci., Kyoto Univ., Kyoto, 606, Japan
SOURCE: Journal of Biochemistry (Tokyo, Japan) (1979), 85(6), 1531-7
CODEN: JOBIAO; ISSN: 0021-924X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The formation of cholesta-7,24-dien-3β-ol (I) and its activity as a substrate for the sterol sidechain methyltransferase in yeast were studied. Expts. with acetone-powder exts. of yeast showed that the sterol is formed from zymosterol by Δ8-Δ7 isomerization. However, direct conversion of I into zymosterol could not be demonstrated. The reversibility of the reaction was proved by the detection of 3H-incorporation into cholest-8-en-3β-ol (with lathosterol as a carrier) from 3H2O in the medium. Incubation of I and S-adenosyl-L-methionine-methyl-14C with the acetone-powder ext. resulted in methylation of the sterol to form episterol. Similar incubation of zymosterol gave fecosterol and episterol, suggesting that fecosterol

initially formed by the methylation was isomerized to episterol. In intact cells, however, an alternative pathway (zymosterol → I → episterol) may also operate. The relative importance of 2 pathways is not known.

L6 ANSWER 42 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1979:34816 CAPLUS
DOCUMENT NUMBER: 90:34816
TITLE: Metabolic profiles on fungi treated with systemic fungicides - a new approach
AUTHOR(S): Whalley, P. R.; Greenaway, W.; Ward, Susan
CORPORATE SOURCE: Bot. Sch., Oxford Univ., Oxford, UK
SOURCE: British Crop Protection Conference--Pests and Diseases, Proceedings (1977), (1), 79-85
CODEN: PBCDDQ; ISSN: 0144-1612
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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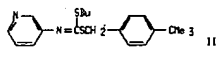
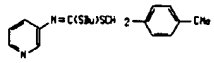


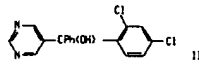
II

AB In a study of the effects of EL 222 (I) [60168-88-9] and S 1358 (II) [51308-54-4] on sterol metab. of Ustilago maydis, I was a strong inhibitor of the enzyme responsible for the 4-demethylation of obtusifoliol [16910-32-0], and II was a weak inhibitor of the enzyme responsible for 4-demethylation of 24-methylene-4,4,14α-trimethyl-5-α-cholest-8-en-3β-ol [6890-88-6]. The ED50 of I and II to U. maydis was 3 and >100 μM, resp.

L6 ANSWER 43 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1977:417055 CAPLUS
DOCUMENT NUMBER: 87:17055
TITLE: Mode of action of the fungicide, Denmert (S-1358) in fungi. Part III. Selective inhibition of the demethylation at C-14 in ergosterol biosynthesis by the fungicide, Denmert (S-1358)
AUTHOR(S): Kato, Toshiro; Kawase, Yasuo
CORPORATE SOURCE: Pestic. Div., Sumitomo Chem. Co., Ltd., Hyogo, Japan
SOURCE: Agricultural and Biological Chemistry (1976), 40(12), 2379-88
CODEN: ABCHA6; ISSN: 0002-1369
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



II

AB In cell-free homogenates of Saccharomyces cerevisiae, Denmert (I) [51108-54-4] inhibited the incorporation of radioactivity from DL-mevalonate-2-14C into 14-demethyllanosterol [2550-84-7], 4α-methylcholesta-8,24-dien-3-one [61849-93-2], 4α-methylzymosterol [7448-03-5], and 4-demethyl sterols (zymosterol [128-33-6] and episterol [474-68-0]) at a concn. of 10-4M. Concomitantly, a large accumulation of radioactivity was observed in the anosterol [79-63-0] fraction. I inhibited the conversion of 14C-labeled lanosterol to 4-demethyl sterols, whereas the conversion of 14C-labeled 14-demethyl-lanosterol to 4-demethyl sterols was hardly affected by the fungicide. It is therefore evident that I is a potent selective inhibitor of the demethylation at the C-14 position in ergosterol [57-87-4] biosynthesis. The fungicide triarimol (II) [26766-27-8], was also found to exhibit the same effect on sterol biosynthesis as I.

L8 ANSWER 44 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1974:67788 CAPLUS
DOCUMENT NUMBER: 80:67788
TITLE: Kinetic properties of S-adenosylmethionine:Δ24-sterol methyltransferase enzyme(s) in mitochondrial structures of Saccharomyces cerevisiae
AUTHOR(S): Bailey, R. B.; Thompson, E. D.; Parks, L. W.
CORPORATE SOURCE: Dep. Microbiol., Oregon State Univ., Corvallis, OR, USA
SOURCE: Biochimica et Biophysica Acta, Enzymology (1974), 334(1), 127-36
CODEN: BBEZAD; ISSN: 0924-1086
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The inhibition of S-adenosylmethionine:Δ24-sterol methyltransferase (EC 2.1.1.41) activity by endogenous cellular components was studied in vitro. The principal inhibitors were Na+ and K+; Ca+, NH4+ and Li+ were also shown to inhibit the reaction. The possible significance of inhibition by Na+ and K+ is discussed. Evidence is presented for the presence of more than one enzyme capable of methylating sterols in cell-free exts. of yeast. Three enzymic activities are described which differ in their respective Michaelis consts. for S-adenosyl-L-methionine, pH optima, and affinity for zymosterol. Based on differences in the apparent Michaelis consts. for zymosterol, it appears that only one may be responsible for in vivo methylation of this ergosterol precursor.

L8 ANSWER 45 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1970:9411 CAPLUS
DOCUMENT NUMBER: 72:9411
TITLE: Isolation and purification of an S-adenosylmethionine: Δ24-sterol methyltransferase from yeast
AUTHOR(S): Moore, J. Thomas, Jr.; Gaylor, James L.
CORPORATE SOURCE: Cornell Univ., Ithaca, NY, USA
SOURCE: Journal of Biological Chemistry (1969), 244(23), 6334-40
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Prepn. of a sol., highly purified S-adenosylmethionine-dependent sterol methyltransferase from yeast subcellular particles is described. The

solubilized enzyme has been purified >600-fold by a no. of procedures. Transmethylation yields stoichiometric amts. of zymosterol consumption and of 24-methylene-dihydroxymosterol (fecosterol) formation. Fecosterol has been identified by a variety of phys. and chem. methods. Glutathione, Mg++, and a neutral pH are requirements for max. activity of the methyltransferase. The value for Km for zymosterol is 6.2 × 10-5M. The enzyme is stable during storage as an (NH4)2SO4 ppt. at -25°. Addnl. properties of the enzyme are described.

L8 ANSWER 46 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1966:492318 CAPLUS
DOCUMENT NUMBER: 65:92318
ORIGINAL REFERENCE NO.: 65:17310d-f
TITLE: Enzymic isomerization (Δ8 → Δ7) of intermediates of sterol biosynthesis
AUTHOR(S): Gaylor, J. L.; Delwiche, C. V.; Swindell, A. C.
CORPORATE SOURCE: Cornell Univ., Ithaca, NY
SOURCE: Steroids (1966), 8(3), 353-63
CODEN: STEDAM; ISSN: 0039-128X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Isomerization of Δ8 to Δ7-sterols by rat liver microsomes was studied under appropriate conditions to eliminate concomitant demethylation reactions. Various proposed intermediates of lanosterol demethylation were incubated with the microsomal prepn. The rates of isomerization of Δ8,24-cholestradienol and Δ8-cholestenol were maximal. The rates of isomerization of 4α-methyl-Δ8,24-cholestradienol and 4α-methyl-Δ8-cholestenol were about 75% of the rates of isomerization of the 4-normethyl sterols. 4,4-Dimethyl-Δ8-cholestenol was isomerized much less rapidly (~30%). The presence of the 14α-methyl group of 4,4,14α-trimethyl-Δ8,24-cholestradienol (lanosterol), 4,4,14α-trimethyl-Δ8-cholestenol, and 14α-methyl-Δ8-cholestenol completely prevented isomerization. Various Δ7-sterols and 3keto sterols remained unchanged. Thus, enzymic Δ8 → Δ7 isomerization of methyl intermediates of lanosterol demethylation may occur, but the rate of isomerization may not be significant until later stages of demethylation are reached. Because acid-catalyzed isomerization was both reversible and active with 14α-methyl sterols, the mechanisms of enzymic and acid-catalyzed isomerization may be different. 19 references.

L8 ANSWER 47 OF 47 CAPLUS COPYRIGHT 2007 ACS on STN
Full Text
ACCESSION NUMBER: 1963:67587 CAPLUS
DOCUMENT NUMBER: 58:67587
ORIGINAL REFERENCE NO.: 58:11611a-c
TITLE: Ketonic intermediates in the demethylation of lanosterol
AUTHOR(S): Lindberg, M.; Gautschi, F.; Bloch, Konrad
CORPORATE SOURCE: Harvard Univ.
SOURCE: Journal of Biological Chemistry (1963), 238, 1661-4
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The transformation of Δ8,24-lanostadien-3-one, of 4,4-dimethyl-Δ8-cholesten-3-one to cholesterol in liver homogenates is demonstrated. Several doubly labeled sterols contg. H3 in the 3α-position and C14 introduced by biosynthesis have been prepd. On conversion to cholesterol, lanosterol-3α-H3 loses 100%, 4,4-dimethyl-Δ8-cholestenol-3α-H3 90%, and zymosterol-3α-H3 20 to 40% of the tritium label. 4α-Methyl-Δ8-cholestenol-2-H3 is efficiently converted to cholesterol; the corresponding 3α-H3 stenol yields only insignificant amts. of labeled cholesterol. The results demonstrate that the formation of 3-ketones is a significant and possibly obligatory reaction in the transformation of lanosterol to cholesterol.

=> d his

(FILE 'HOME' ENTERED AT 18:06:02 ON 09 FEB 2007)

FILE 'REGISTRY' ENTERED AT 18:06:11 ON 09 FEB 2007
L1 1 S 7448-02-4
L2 1 S 128-33-6

FILE 'AGRICOLA, ALUMINIUM, ANABSTR, APOLLIT, AQUALINE, AQUIRE, BABS, BIOTECHNO, CABA, CAOLD, CAPLUS, CBNB, CEABA-VTB, CERAB, CIN, COMPENDEX, CONFSCI, COPPERLIT, CORROSION, DISSABS, ENCOMPLIT, GENBANK, INSPEC, INSPHYS, IPA, JICST-EPLUS, KOSMET, METADEX, ...' ENTERED AT 18:10:52 ON 09 FEB 2007
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L4 40 DUP REM L3 (1 DUPLICATE REMOVED)
L5 17 S L4 AND (OXIDASE OR OXYGENASE OR METHYLASE OR DEMETHYL? OR ME
L6 126 S (L1 OR L2) AND (OXIDASE OR OXYGENASE OR METHYLASE OR DEMETHYL
L7 109 S L6 NOT L3
L8 47 S L7 AND (DEMETHYLAT? OR METHYLAT?)

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